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June 1961

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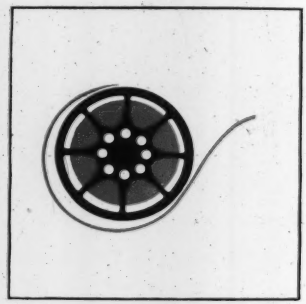

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CONSULTANT welcomes questions and comments about any of the topics covered. The authors will answer all questions by mail, and some of the most informative replies will be published in this section. Please address all correspondence to CONSULTANT, SK&F Laboratories, 1500 Spring Garden Street, Philadelphia 1, Pa.

Sinusitis in Children

(Consultant, April '61)

Sir:

This afternoon I received a copy of the first number of CONSULTANT. I am glad to tell you that I think it is a wonderful little journal. Every article is practical. Keep it that way. Most of the articles in most of the journals are above and beyond the heads of most of us doctors, even the young ones.

I would like to comment on Dr. Seltzer's article: I would not have waited 10 days to open the child's maxillary sinus. I wouldn't have waited more than 2 or 3 days. Cocaine is too dangerous (if a patient is hypersensitive to it) to use in 10% solution. 4% solution is strong enough even for submucous resections. I would use a rasp in place of a needle —the rasp through the "soft spot." That leaves an opening in the antral wall that will stay open a week or so, allowing daily irrigation. No anesthetic is needed after the original puncture. I would not have put the hospital bill on the child's family or us taxpayers. I'd have treated her in my office or maybe the first two visits in the home.

The value of fresh air in treatment of sinusitis should be stressed. Unless the patient is pretty sick he should spend a few hours daily outdoors, wrapped up warmly, of course, and not in rain or fog. The overheating of homes is a powerful cause of bad colds and sinus infection and a deterrent to treatment . . .

—J. J. Horton, M.D.
Buda, Texas

Doctor Horton's points are well taken, and in what might be called an "average" patient I am largely in agreement. In this case, however, parental objections caused delay in making the puncture, and the patient was so sensitive to pain I felt 10% cocaine was needed. Before using stronger solutions, I test by spraying the nasal cavity lightly with 1% cocaine and wait about 20 minutes to make sure there is no hypersensitivity. I prefer to use a needle initially, instead of a rasp, because the puncture is, in a sense, diagnostic. I use a rasp only when natural drainage can't be induced and pus continues to form. Hospitalization is valuable in case an emergency should develop, and from a medico-legal standpoint.

—Albert P. Seltzer, M.D.

Apathy in the Aged

(Consultant, April '61)

Sir:

I agree with Dr. Bortz that apathy in older people is an increasingly important problem and may be said to be the basis of many ills . . . It is interesting to read constantly in similar articles that man should now get interested in something. If he were better prepared in early life this would come almost as a continuation of an interest throughout a lifetime. Now it would be even more interesting—it would reach a point of final development. I feel that there is no better way to get rid of a feeling of apathy than by constantly improving oneself. This however can be done only with an early start.

I would also like to ask Dr. Barness a question about hypernatremia: Do you feel that as soon as dehydration or an electrolyte imbalance of any type is suspected, it would be wise to hospitalize the child for most efficient treatment? I feel that too often a tragic result occurs because of waiting too long.

—Adolph F. Borkowski, M.D.
Philadelphia

Hypernatremia in Children

(Consultant, April '61)

Reply to Dr. Borkowski's question:

Mild diarrhea and mild dehydration are seen almost daily in pediatric practice. I would recommend hospitalization only when the child has generalized illness in addition to his diarrhea. Tragic results can be avoided by more thorough observation of the child, with better recognition of impending illness, rather than routine hospitalization.

—Lewis A. Barness, M.D.

Air-Swallowing

(Consultant, April '61)

Dear Dr. Roth:

I read with great interest your article on Air-Swallowing in the April 1961 issue of the Consultant.

The reasoning of aerophagia has always been a puzzle to me. It is my contention that if there is such a condition as aerophagia, it should be possible to reproduce this con-

dition in normal individuals who do not complain of gastrointestinal disorders.

I have made repeated tests on myself and others trying to swallow air with and without food or drinks . . . As yet, I have not been able to reproduce aerophagia . . .

. . . I think it is a well known fact that scientifically it is the tendency of air to rise, even in the body . . . (and) I just can not bring myself to believe that food can push air from the stomach into the large intestine which is at least 20-22 feet removed from the stomach.

In my observations and experiences . . . gas in the gastrointestinal tract is caused only by a faulty mechanism in the path of this tract . . .

I have not been able to find anything in the literature which would put aerophagia on a scientific basis. I would appreciate it, if you could suggest any scientific work done on aerophagia.

Thank you.

–E. K. Bell, M.D.
Bryan, Ohio

Whether or not an individual patient can have symptoms attributed to aerophagia reproduced under experimental circumstances depends upon a number of factors; namely, the amount of air and rapidity with which it is introduced, the degree of tone in the gastrointestinal tract at the time (tension of the patient), crowding of the stomach by adjacent viscera (e.g. a simultaneously distended splenic flexure), presence of stomach cascading, the patient's threshold for discomfort and other factors. In one of my patients it was necessary to introduce air by way of nasogastric tubes into the stomach and simply inflate air into the stomach flexure per rectal tube before the symptoms could be reproduced.

There is considerable evidence to indicate that swallowed air is the chief source of gastrointestinal "gas". Swallowed air is credited with contributing approximately 70% of intestinal "gas"; diffusion of gases from blood stream accounts for 20%; and bacterial decomposition of food residue produces about 10% of intestinal gases (Wangensteen). Maddock has shown during pyelography that: (1) considerable amounts (45 to 1345 cc) of external air (proved by gas analysis) could be aspirated from the stomach during a one hour procedure; (2) if continuous suction were applied to the stomach, no increase in the amount of intestinal "gas" appeared on subsequent serial x-ray films; and (3) three times more air was aspirated from the stomach of nervous patients than from those who were calm. It has also been shown that air introduced into the stomach may pass through the small intestines to the cecum in about 10 minutes which result in the passage of flatus in about 30 minutes. Food doesn't "push air" through the gastrointestinal tract, but peristalsis can carry a "bolus of air" around the food and fecal residues. References to the subject of aerophagia may be found in the MEDICAL CLINICS OF NORTH AMERICA, November 1957. pages 1673-96.

–James L. A. Roth, M.D.

Dear Dr. Roth:

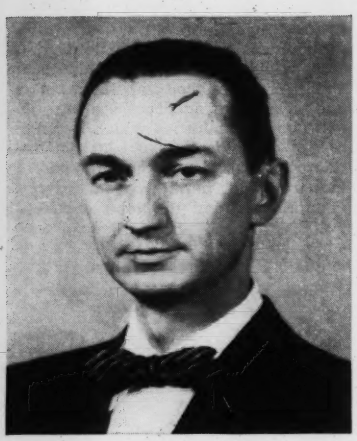
What is the value of sublingual nitroglycerin as a therapeutic test for pseudo-angina? Also, how can one clinically differentiate symptoms due to magenblase from those due to splenic flexure involvement, i.e., without x-ray?

–Seymour Piwoz, D.O.
Philadelphia, Pa.

Unfortunately the response to nitroglycerin will not differentiate between the pain caused by aerophagic pseudo-angina and that caused by angina pectoris or hiatus hernia, for as a smooth muscle relaxant (vascular or gastrointestinal) nitroglycerin will relieve pain due to all three. Pain of angina pectoris may be relieved somewhat more promptly, but this difference in the rate of response is a relative one and its value as a therapeutic test is limited.

Differentiating between the magenblase syndrome and splenic flexure involvement is difficult because the gastric air bubble and the splenic flexure accumulation of gas both cause left, upper abdominal fullness, pressure, etc., that may be relieved with either belching or evacuation of the colon. However, *immediate* postprandial fullness, relieved most effectively by *belching* favors the magenblase syndrome, and the larger area of tympany associated with it will be located chiefly in the *mid-epigastrium.* On the other hand, in the splenic flexure syndrome, the left upper quadrant fullness and distress is experiencd *later* after meals and is relieved most effectively by expulsion of flatus, bowel movement or enemas. The area of tympany in the splenic flexure syndrome is located more to the left of the mid-line, in the *lateral left upper quadrant.*

–James L. A. Roth, M.D.



James R. Jude, M.D.
Johns Hopkins Hospital

James R. Jude is Chief Resident in Surgery at The Johns Hopkins Hospital in Baltimore where he, William B. Kouwenhoven, Dr.Ing., and G. Guy Knickerbocker, M.S.E., developed the technique of external cardiac massage. Dr. Jude received his medical training at the University of Minnesota Medical School. He has co-authored more than 20 scientific articles and has received several scholarships and awards, the most recent being the Mead-Johnson Award for Graduate Training in Surgery, 1959-1961. Dr. Jude's special interest is thoracic and gastrointestinal surgery.

HOW TO PERFORM CLOSED-CHEST CARDIAC MASSAGE

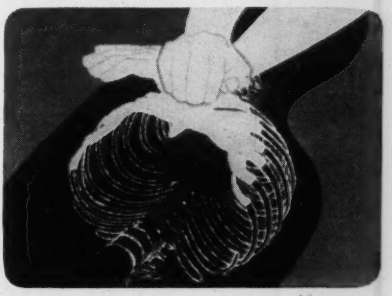
This article describes a technique that can be used to start hearts beating again in victims of sudden cardiac arrest. It is a technique we have used to restore functional cardiac activity and pre-arrest central-nervous-system status in 61% of more than 100 patients whose hearts had abruptly stopped beating.

Both ventilation and circulation are necessary to sustain life, and both must be maintained by artificial methods when they are interrupted. Mouth-to-mouth respiration can be used to restore and maintain ventilation, and we now know that it is possible to massage the heart, to restore and maintain circulation, *without* opening the chest. This method makes it possible for the physician to attempt cardiac massage anywhere at all, using only his two hands.

Essentially, the method consists of closed-chest cardiac massage—manual application of rhythmic pressure to the patient's lower sternum—and ventilation of the lungs by mouth-to-mouth respiration. Since death or irreparable damage to the brain may occur within 4 to 5 minutes, the wisest course is to *act at once*, without further examination, if cardiac arrest is even suspected. Removal of clothing, except for outer garments, and confirmatory diagnostic procedures are time-consuming and unnecessary. The patient should be placed supine on a firm surface such as the floor. The physician should make sure there is a patent airway by tilting the patient's head back, and he should insufflate the lungs a few times. If this is not sufficient to return signs of life, then external cardiac massage should be initiated at once.

Make sure there is a patent airway, and ventilate the patient's lungs.

Begin cardiac massage. Apply *forceful* pressure 60 to 80 times a minute on the lower sternum. Do not apply any pressure on the ribs with your fingers; use only the heel of the hand.



By pushing the lower sternum 1 to 1½ inches posteriorly, you compress the heart between it and the thoracic vertebral column, and blood is forced into the pulmonary and systemic circulatory systems. When you release the pressure, the patient's chest will expand, and his heart will refill with venous blood.

In adult men and women, the proper place to put the heel of your hand is on the sternum just above the xiphoid. Use both hands, one on top of the other.

In children up to nine or ten, you need only use the heel of one hand for pressure since their rib cage is very flexible.

In infants, you should apply pressure only with the fingertips of one hand to avoid damage to the liver or other internal organs.

OUTSIDE THE HOSPITAL (CONTINUED)

Insert "S" tube, if available, to facilitate mouth-to-mouth breathing. If alone with the patient, you should interrupt massage every 30 seconds to ventilate his lungs two or three times.

If a third person is present, have her call for an ambulance and alert the hospital that the patient is a cardiac arrest victim. Then tell her to breathe regularly (12 to 14 times per minute) into the patient's mouth while holding his nose closed. Give an intracardiac injection of epinephrine (0.5 mg.) if heart action has not resumed after a few minutes.

Continue massage and mouth-to-mouth breathing while patient is on the way to the hospital.

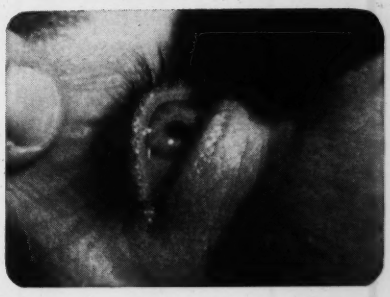
NOTE: The photos accompanying this article are excerpts from a new SK&F medical motion picture, EXTERNAL CARDIAC MASSAGE, by James R. Jude, M.D., W. B. Kouwenhoven, Dr.Ing., and G. Guy Knickerbocker, M.S.E., of the Johns Hopkins Medical Institutions. The film is available through SK&F Representatives, or may be obtained by writing to the SK&F Medical Film Center, 1500 Spring Garden Street, Philadelphia 1, Pa.

If respiration has not returned, intubate the trachea and begin positive pressure ventilation. Continue massage.

Apply external defibrillator if EKG shows patient's heart to be in ventricular fibrillation. Since weak fibrillation is not easily converted to sinus rhythm, it may be necessary to inject dilute epinephrine directly into the heart to strengthen the ventricular fibrillation.

If a regular intravenous needle cannot be inserted, do a venous cutdown as soon as possible since continuous use of vasopressors may be necessary to maintain an adequate blood pressure.

Once you have started massage, the vital signs to look for indicating adequate circulation are spontaneous gasping respirations, palpable brachial, carotid or femoral pulses, and constriction of the pupils.



PSYCHIATRY

Gwyn H. Lile, M.D.
University of Chicago

Gwyn H. Lile is Assistant Professor of Psychiatry at the University of Chicago School of Medicine. He received his degree from Harvard Medical School and his residency training at the Massachusetts Mental Health Centers, and at the University of Chicago Clinics. He is particularly interested in psychosomatic medicine and is currently investigating the physician-patient relationship in peptic ulcer. He is a member of the Illinois and the American Psychiatric Associations, and contributed a chapter to the recently published book WORKING WITH SUPERIOR STUDENTS: THEORIES AND PRACTICES (Science Research Associates).

PSYCHOGENIC IMPOTENCE

Impotence is a symptom, not a disease. As it does for any symptom, rational treatment depends on the identification and elimination or control of the underlying cause. When the cause is organic (as it is only about 10% of the time) it can usually be uncovered by thorough physical and neurological examinations and routine laboratory tests, and the physician can determine what the appropriate treatment should be. Psychogenic impotence, however, seems to pose more of a problem to the average physician.

The stimulus that triggers sexual arousal and erection is psychological. Because this stimulus is delicate and easily inhibited, sexual arousal requires freedom from external or internal interference. Anxiety, anger, and depression can all interfere with it, and the underlying cause of psychogenic impotence is the inappropriate presence of one of these emotions. The problem, then, is to determine which of these emotions is intruding, and to eliminate it.

A mistake in timing is often made with these patients. The physician takes a history, does a physical examination, and then confronts the patient with negative evidence, tells him that nothing is wrong with him, and that he should see a psychiatrist. The patient, already suffering shame or anxiety, often reacts with intense resentment which interferes with his willingness to cooperate with psychotherapy. You can minimize this reaction simply by discussing the positive information you find in the history *before* you perform the physical examination. If the physical examination is negative, you are then in a

much better position to help the patient overcome his problem, or help him realize that he should consult a person trained to deal with it.

As a start, find out in detail what the specific complaint is: inability to have or maintain an erection; premature or retarded ejaculation; or lack of sexual desire or pleasure. Then ask about the circumstances surrounding intercourse and how long the complaint has been present. As the patient talks, note his attitude toward the symptom – shame, panic – and try to estimate the amount of sexual anxiety. For example, ask about his pre-marital dating experience—either too little or too much suggests an abnormal amount of sexual anxiety. Inquire about the sex education he has received and from whom; his attitude concerning masturbation; his marital history. Since the patient will almost always be uncomfortable, indirect rather than direct questioning is usually more productive. Don't ask the patient if he masturbates, but how he feels about it. Similarly, don't ask how he gets along with his wife – he is almost certain to say he gets along fine – but ask him to describe her as a person and how he met her. Actually, listening to how the patient says things is often more informative than what he says; e.g., if he gets restless and keeps looking at his watch when you ask about his wife, or seems to take offense, marital discord may be a problem that he cannot admit, even to himself. When you have this information, you should be able to differentiate five syndromes of psychogenic impotence.

1. Situational anxiety

The chief, usually the only, complaint is failure or loss of erection. The problem is acute; he will have had only one or two failures. If he has had more, or has other sexual complaints, he does not have situational anxiety. Symptoms of anxiety (tachycardia, sweating palms) may be reported. Although some shame may also be present, his primary attitude will be one of frantic concern. His sexual history is relatively normal. The key to the diagnosis is in the circumstances surrounding the incident. For example, a newly married couple living with parents: the solicitous mother-in-law comes to their bedroom and tells them to just whisper if they need anything and she'll hear them. The honeymoon is a difficult time for most men, what with excitement, alcohol, and tensions, and "honeymoon fatigue" is so common that a little impotence on the honeymoon is almost par for the course.

Discussion and reassurance that failure was entirely normal under the circumstances is usually all the treatment that is required. The patient obviously should not be referred to a psychiatrist.

2. Failure anxiety

This syndrome is a consequence of uncorrected situational anxiety. The patient has the same complaints but the problem will have persisted longer, maybe for about a month. His attitude will have changed from frantic concern to humiliation, and you will usually find greater evidence of anxiety or guilt in his sexual history. His past failure has created a fear of continued failure and perhaps a fear that his wife is laughing at him or is disappointed in him. Consequently, even though the circumstances that caused the situational anxiety may have disappeared, he continues to fail.

Treatment is again relatively easy. Discussion, reassurance, and explanation that the initial failure has produced the fear of further failure may suffice, but you may have to repeat your explanations on several occasions. As a psychological crutch, you can prescribe a medication to be taken half-an-hour or so before intercourse – phenobarbital or almost any mild sedative – and you may have to discuss the problem with the wife. Normal relations are usually established quickly after one successful intercourse. The patient need not be referred.

3. Neurotic anxiety

This syndrome is the result of long-term conditioning of the sexual response, and the patient fails because any kind of sexual thought causes him anxiety. He may not be able to have or maintain an erection, or may report premature or retarded ejaculation. He will not be able to tell you why because the reasons are hidden from his awareness. In addition to minor symptoms of anxiety he may have phobias, obsessions, hypochondriasis or neurasthenia. His attitude may be surprisingly blasé but is often subtly resistant. For example, he may insist on immediate relief, but, refuse to go to a psychiatrist. His history may reveal perversions, and in any case, you will usually find a history of considerable anxiety and guilt. This patient should be referred to a psychiatrist.

4. Hostility to wife

The main complaint varies. It may be failure to have or maintain erection. Retarded ejaculation in a patient who has had normal relations for a while is almost always a sign of hostility. These patients often report headaches and miscellaneous pains or muscular weakness. The problem may be acute (failure after a squabble) or chronic. Infidelity is often a problem. He may admit that he masturbates. His sexual history may or may not be normal, and he may have a somewhat self-centered, paranoid, or dependent personality. His attitude may be any one of several. He may say that he has no interest in treatment, or blame his wife for the problem; he may want treatment only so his extra-marital affairs will be successful; or he may say that "if there *is* a treatment, maybe I *should* take it, but I hope it doesn't hurt too much." This patient should be referred to a psychiatrist or competent marriage counsellor.

5. Depression

This patient will have been unable to maintain an erection or unable to have one for up to six months or more; he often says he has "no sexual desire at all." He feels blue, can't concentrate, and in addition to impotence, will almost always complain of one or more of the other physiologic symptoms of depression: insomnia, constipation, or anorexia. His past history will usually be fairly normal, but he often launches into a detailed confession of his minor transgressions—the time he went out with a prostitute when he was 16, the time he had intercourse before he was married. His attitude is usually self-accusatory; he feels hopeless and he may be suicidal. If he is suicidal, he should be hospitalized for his own protection. If the depression is not too severe, you may want to manage him yourself with one of the new anti-depressant drugs, or his depression may be severe enough to make you want to refer him to a psychiatrist. When in doubt, it is safer to refer him.

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Prescribing information adopted January 1961.

OBSTETRICS

Edwin J. DeCosta, M.D.
Northwestern University

Edwin J. DeCosta is Associate Professor of Obstetrics and Gynecology at Northwestern University Medical School and attending obstetrician and gynecologist at Passavant Memorial Hospital and Cook County Hospital in Chicago. After receiving his medical degree from Rush Medical College, he took his residency at Cook County Hospital and Michael Reese Hospital. Dr. DeCosta is a Fellow of the American College of Surgeons and a member of the American College of Obstetrics and Gynecology, the American Association of Obstetricians and Gynecologists, and the American Gynecological Society.

CAN YOUR PRENATAL CARE BE IMPROVED?

Twenty-five years ago we were sure that the last word had already been written on prenatal care. At that time, we paid attention to the pregnant woman's diet, weight gain, blood pressure, blood count, urine, the tonsils and teeth and the heart and lungs, as well as to the position and presentation of the fetus and the size and configuration of the pelvis. The result of these efforts, and of better delivery care, was the startling reduction in deaths among the mothers to about 50 per 10,000 live births (white women) by 1935 in the United States.

Since then, maternal mortality has dropped to an almost unbelievable 3 deaths per 10,000 live births, largely because of improvements in prenatal and ancillary care. There is not much maternal mortality left to reduce, but there are certain aspects of prenatal care that are still too often neglected and yet are important to the health and happiness of both the mother and child.

Emotional Preparation For Childbirth

I think we sometimes forget that pregnancy is an emotional experience as well as a physiologic experience. Every woman fears for herself and for her baby. She worries about reaching the hospital in time, about paying the hospital bills, about caring for her baby. Many women fear that they may have an abnormal baby. Some may have guilt feelings for not wanting a baby, or for not loving their husband. All of these emotional factors are important and, if possible, should be discussed in an effort to reduce anxiety by giving the patient personal attention and counsel and, when warranted, by enlisting expert psychiatric aid.

Education of the primagravida is particularly important. She should be told what labor is like, that she will have contractions, that she may bleed, that she may lose fluid. Preferably, she should visit the labor suite and nursery before her admission to the hospital. To avoid difficulties with anesthesia, she should be warned against eating or drinking after the first signs of the beginning of labor. Attention to these details may seem hardly worth stressing, but they are too often neglected for one reason or other. Loving care will be rewarded by happier, easier labor, appreciated by the patient, her family and, incidentally, her doctor, too.

Blood Types

In recent years, most of us have paid attention to the Rh factor in the mother's blood. However, a goodly number of us ignore ABO sensitivities. Erythroblastosis may result from ABO factors just as they do from Rh. All patients should have their blood typed, and the husbands of type O women should be checked. If the husband is A, B or AB, cord blood should be drawn at the time of the baby's birth to determine the baby's blood type and antibody titre and to establish a base line of serum bilirubin and blood count. If the baby is other than O, we must watch for jaundice, increase in bilirubin, and drop in the R.B.C. Replacement transfusion may be a life-saving measure for these children.

Preventive Medicine

Another phase of prenatal care which we tend to overlook is the opportunity for really practicing preventive medicine. This is the period of magnificent rapport with our patients, and they will usually follow our advice. We may detect dental caries, pulmonary tuberculosis, syphilis, and emotional disturbances, just to mention a few. But in addition we are given the chance to vaccinate against poliomyelitis, and, probably most important of all, to seek out and treat early cervical carcinoma. We should not permit the youthfulness of our patients to dissuade us from making a thorough examination. I am inclined to consider the Pap smear even more important than the Kahn test. Leastwise, in my practice I see many more abnormal Paps than positive Kahns.

Although admittedly a controversial subject, we think of carcinoma *in situ* as a true intra-epithelial cancer and therefore the eventual forerunner of invasive cancer. About 20% of these changes seem to be reversible, but we do not gamble on the wishful anticipation that the mucosa will return to normal. I follow these patients closely with repeated biopsy; I feel that a diagnosis must be established even if this requires conization of the cervix during pregnancy. If the diagnosis of invasive cancer is made, the patient must be treated the same as any patient with cancer, ignoring the pregnancy but not ignoring the malignancy. This does not mean that a viable fetus should be sacrificed, but it does mean that treatment should not be delayed if the diagnosis of cancer is made early in pregnancy.

These are some of our newer concepts of prenatal care. In the future, others are sure to be added, but we should always remember that common sense is all-important and that most pregnant women are just a bit frightened and need moral support.

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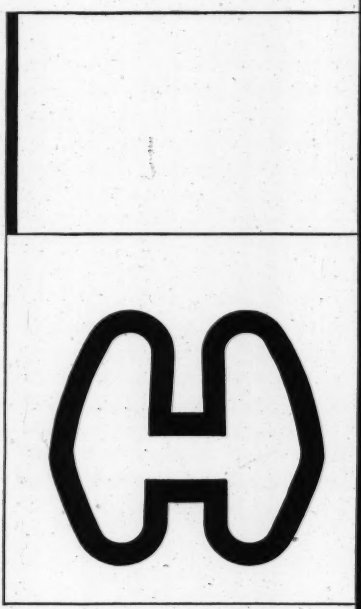
4. Value as a diagnostic aid
5. Effectiveness in many thyroid-resistant patients



PRESCRIBING INFORMATION

ADMINISTRATION AND DOSAGE: Dosage should be adjusted according to the severity of the condition and the response of the patient.

Most patients should be started on 25 mcg. of 'Cytomel' daily. To increase dosage to recommended maintenance levels for these patients, increments of 12.5 or 25 mcg. may be made in the daily dosage at intervals of one or two weeks. Dosages in the range of 100 mcg. daily, and higher, are well tolerated by many patients.

When starting dosage is 5 mcg. daily (as in myxedema, male infertility, simple goiter and in patients being switched from thyroid, L-thyroxine, or thyroglobulin), increments of 5 or 10 mcg. may be made in the daily dosage at intervals of one or two weeks. When dosage reaches 25 mcg. daily, increase as described above.

'Cytomel' is usually administered in divided doses.

Note: In geriatric patients or in children always start with 5 mcg. daily and adjust dosage in increments no greater than 5 mcg.

Indication	Recommended Starting Dose	Recommended Maintenance Dose
Hypometabolism Mild Hypothyroidism	25 mcg. daily	25-75 mcg. daily (Smaller doses may be fully effective in some patients.)
Myxedema	5 mcg. daily	50-100 mcg. daily
Female Reproductive Disorders	25 mcg. daily	25-50 mcg. daily
Male Infertility (Based on sperm count or sperm motility responses after two to four weeks of treatment at a given dosage level, the daily dosage may be increased by 5 or 10 mcg. If after further treatment the desired response has still not been obtained, the daily dosage may again be increased. Although total daily dosage usually need not exceed 25 mcg., as much as 50 mcg. daily may be used if necessary.)	5 mcg. daily	10-25 mcg. daily
Simple (non-toxic) Goiter	5 mcg. daily	25-75 mcg. daily

SPECIAL CONSIDERATIONS AND CAUTIONS: Tachycardia, excitability, headache, or excessive sweating are signs of overdosage. Medication should be interrupted until the unpleasant symptoms disappear, and then resumed in smaller doses. Since the return to pretreatment status is rapid, 'Cytomel' can usually be resumed at the desired dosage after one to two days.

When a subnormal BMR exists as part of the clinical syndrome of hypometabolism or hypothyroidism, administration in excessive dosage will cause elevation of BMR to levels above normal.

'Cytomel', unlike various forms and fractions of thyroid, will not cause elevation of the blood protein iodine level.

Endogenous thyroid gland function, reflected particularly by I^{131} uptake, may be depressed by 'Cytomel' administration. Depression of this function is most apt to occur with higher dosages (greater than 75 mcg. daily). Experience to date indicates that this effect is not clinically harmful. There have been no unfavorable sequelae in reported instances where 'Cytomel' therapy has been discontinued after depression of I^{131} uptake occurred. In such cases this function has promptly returned to normal after discontinuance of 'Cytomel'.

Since 'Cytomel' is physiologically related to thyroxine, it is not recommended for use in the presence of angina pectoris, in other cardiovascular disorders, or ischemic states. However, if it is used in the presence of such conditions, the starting dosage should never be more than 5 mcg. daily. If dosage is increased, it should be in increments of no more than 5 mcg. daily at approximately two-week intervals.

Hypopituitarism, morphologic hypogonadism and nephrosis should be ruled out before 'Cytomel' is administered.

CONTRAINDICATION: Addison's disease.

FORMULA: Each 'Cytomel' tablet contains 5 mcg. or 25 mcg. of liothyronine (L-triiodothyronine or LT3), as the sodium salt; 25 mcg. of 'Cytomel' is calorigenically equivalent to approximately 1 gr. of thyroid.

AVAILABLE IN TWO DOSAGE STRENGTHS: 25 mcg. (scored) tablets in bottles of 100 and 1000; 5 mcg. tablets in bottles of 100.

Prescribing information adopted Jan. 1961

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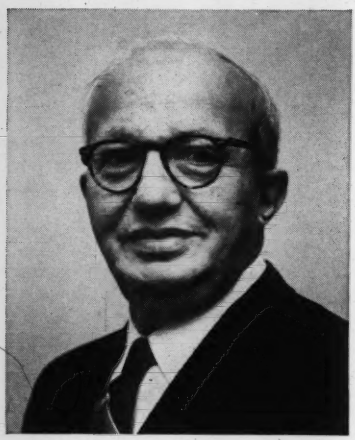

Albert P. Seltzer, M.D.
University of Pennsylvania

Albert P. Seltzer is Chief of the Ear, Nose and Throat Departments at Philadelphia General Hospital and Mercy-Douglass Hospital; senior attending physician at Albert Einstein Medical Center; and Associate Professor of Otolaryngology at the University of Pennsylvania Graduate School of Medicine. In the April issue of CONSULTANT, Dr. Seltzer discussed sinusitis in children. This month, he outlines a practical method for managing a relatively rare–but difficult-to-manage–clinical problem.

ONE WAY TO PACK THE NOSE IN PERSISTENT NOSEBLEED

The fact that almost all nosebleeds can be stopped promptly somehow makes those that cannot all the more frightening.

Take a case I saw during the past winter. This 48-year-old man had been sitting quietly at home when suddenly his nose began to bleed profusely. When his family became frightened at their failure to stop the bleeding by cold compresses, they took him to the hospital, where application of pressure and insertion of ½-inch nasal packing material also failed to help. The patient then became quite disturbed–over two hours having elapsed–and left that hospital and went to another. There his family physician called in a surgeon, who tried postnasal packing with adrenalin and Gelfoam, still to no avail. By now, more than six hours had elapsed; the patient was in critical condition and was receiving a blood transfusion. I saw him a few minutes later and applied and secured both postnasal and anterior packing. This, plus sedation, gradually slowed the bleeding. The anterior packing was left in for five days; the postnasal packing was left in an additional 48 hours to be sure all bleeding had stopped. Later I found a mass on the nasopharynx that proved to be a squamous cell carcinoma.

When cases of this severity occur, a thorough postnasal packing is obviously vitally important. Here is a method I have found effective (if you know some improvements or variations on it, I hope you will write to me). First roll a strip of 1½-inch gauze

tightly like a ribbon to form a roll or cylinder about ¾ of an inch in diameter. Then tie the roll tightly in the middle with two pieces of umbilical-cord material, leaving three ends of the strings about eight to ten inches long.

Push a rubber catheter in through one side of the nose (Fig. 1) until the end appears in the throat, then pull it out through the mouth with a hemostat and tie the end of one piece of string firmly to the tip of the catheter (Fig. 2). Withdraw the catheter back through the nose until the string protrudes (Fig. 3), and untie the string. Then, in order to pull a second string through the other nostril, the catheter must be re-inserted and the procedure repeated on the opposite side. Now a length of string protrudes through each nostril, and the third length protrudes, along with the roll of gauze, through the mouth.

By pulling on the strings which protrude through the nostrils, and simultaneously pressing the roll firmly from behind with a finger inserted through the mouth, you can wedge the packing firmly into place (Fig. 4).

Then place a small gauze pad (or vaseline-coated gauze pad) across the front of the columella (anterior septum) and tie the two ends of string tightly together across the pad. This will prevent ulceration from pressure. The remaining length of string, (the third piece), which is protruding from the mouth, should be pulled (not too tightly against the corner of the mouth) to one side and anchored to the side of the face with a piece of adhesive tape (Fig. 5). When bleeding has stopped, the packing can be removed by cutting the strings tied across the septum

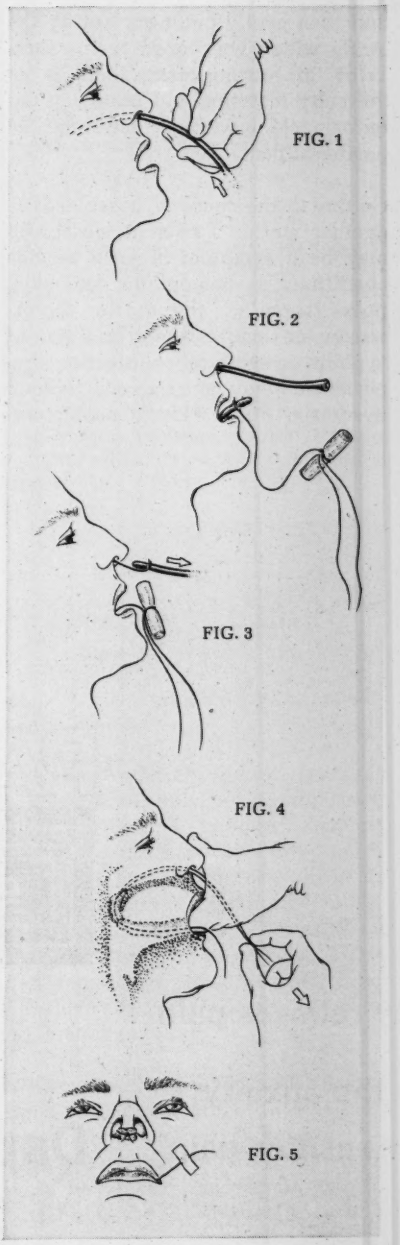

FIG. 1

FIG. 2

FIG. 3

FIG. 4

FIG. 5

and then gently pulling it out by the string which was taped to the face. With this arrangement, there is no difficulty inserting and removing anterior packing without disturbing the postnasal packing.

Getting at the *cause* of nosebleeds is another matter. Persistent nosebleed may be a symptom of such serious conditions as hemophilia, leukemia, polycythemia, rheumatic fever, scurvy, or tumors. It may be a sign of syphilis or some other infection; hypertension may be involved, or blood dyscrasia, or, in elderly people, arteriosclerosis. And it is said that nosebleeds may sometimes be vicarious menstruation.

In children, nose picking (epistaxis digitorum) is a likely cause; so is congestion of the mucous membrane as in measles, whooping cough and scarlet fever. As I say, I try to find the cause of nosebleeds, but I don't always succeed because, in children, the etiological agent is likely to be the patient's brother's fist, and nobody will talk. Whatever the cause, keep the patient under observation to be sure the condition is controlled.

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DOSAGE: 1 tablet every three hours as needed. (With light sleepers the final dose should not be taken so late in the day as to interfere with sleep.)

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AVAILABLE: Unlike most analgesics, 'Daprisal' is available on prescription only. In bottles of 50.

Prescribing information adopted January 1961.

SK&F Daprisal®

PEDIATRICS

F. Michael Smith, Jr., M.D.
St. Joseph's Hospital, Thibodaux, La.

F. Michael Smith, a Fellow of the American Academy of Pediatrics, is Chief of Staff at St. Joseph's Hospital in Thibodaux, Louisiana. He received his medical training at Louisiana State University Medical School, Charity Hospital in New Orleans, and St. Joseph's Hospital in Thibodaux. A past president of the Lafourche Parish Medical Society, he is also a member of the Louisiana State Medical Society and the Louisiana State Pediatric Society. His investigative interest lies mainly in pediatric cardiology; he serves on the Board of Directors of the Louisiana State Heart Association.

LET'S DO AWAY WITH INFANT "COLIC"

In my opinion, there is no other area of fantasy and fiction comparable in magnitude to that of the well baby care of a newborn infant. High on a list of such errors would be "colic" – because there is a continued belief that colic is a specific disease entity, requiring special treatment and special medicine.

Let's look at some of the facts. If one examined the many thousands of case histories in a large hospital such as Charity Hospital in New Orleans, it is doubtful that any could be found with the primary diagnosis of colic. Yet, how many of us in private practice tell our patients their child has colic? Colic never appears in the hospital newborn nursery; yet, almost immediately after the child's arrival at home, the telephone rings at the doctor's office announcing the appearance of colic.

Colic is practically always found in the first-born; only rarely do parents with two or three children complain that their child has colic. Furthermore, the astute and experienced physician can often foretell by the tension and nervousness of the expectant mother that her child will have colic. These being the facts that attend colic, can one logically conclude that it is an organic disease?

What we call "colic" is not a disease but a problem situation in which both parents and child are adjusting to a new environment. The problem of colic has many causes and predisposing factors: these include a long-accepted folklore, and parental

personality factors; most of all, however, the basic problem seems to be a lack of preparation for the responsibilities of parenthood. (Modern society – through the media of television, movies, and books – deceives the prospective parent into expecting an infant who is at all times a restful, lovable, sleeping angel.) Parents are simply not prepared for the day-after-day assault on the nervous system by the crying, straining, struggling, soiled, wet, trembling, hiccuping, bundle of flesh that is man's start on this earth. They are unprepared – emotionally – for the demands that now must be met with personal self-sacrifice to insure their infant's survival.

To make matters worse they are inexperienced, inept, and insecure in their grasp of the day-to-day mechanics of caring for an infant. Their insecurity is especially evident when the baby cries, because to them, every cry signals an emergency and inspires panic. Actually, not all crying is due to pain or gastrointestinal dysfunction. It can have as many meanings as the infant has needs, wants, and reactions. Only think of the loud wail you can stimulate by thumping your finger against the sole of the child's foot and you will realize the normal infant's extreme reactivity to his environment. Loud noises, tight clothing, soiled diapers, and, of course, hunger, will cause a normal infant to cry lustily, loud, and long. Also, many infants cry seeking only human contact, pleasant and harmonious sounds, the warmth and security of being held.

The Language of Crying

It is possible for the seasoned parent to detect numerous variations in the way an infant cries which can be understood almost as readily as language. The experienced parent can tell with reasonable accuracy a cry of hunger from a cranky cry, a cry of bearable discomfort from a lonesome cry, and all kinds, unerringly, from the cry of real distress or pain. Unfortunately, such understanding of the infant's piercing attempts at communication is slowly and painfully learned. In the meantime, panic or impatience leads to uncertain, inconsistent handling and so to an uncertain, often crying infant. Quite understandably, parents feel frustrated and inadequate and long for a pat solution to their responsibilities. They are easy prey, at this time, to the recurring suggestion from relatives and friends that their child has "colic."

So, they consult their physician and seek from him a bottle of "colic medicine" – the magic remedy for all their discomfort. To their chronic misfortune, the harrassed physician too often encourages this error – blocking an intelligent appraisal of the child's crying, and beginning a cycle of problems. Soon the medicine is found ineffective. So, formulae are changed and changed and changed. New medicines are endlessly tried, red drops are substituted for green ones, until time and the infant's maturation eventually solve the problem.

There are many reasons for crying and excessive irritability in the newborn but only rarely do they involve organic disease; of course, all such infants merit careful and complete histories and physical examination. For example, some infants manifest gastrointestinal allergy; in these, a trial of 7-10 days on hypoallergic formula will act both as a therapeutic

and diagnostic measure. Once organic causes have been ruled out, the physician should direct his attention to helping the parents overcome their susceptibility to the colic myth. Here is a method I have found effective in dealing with parents of healthy but "colicky" infants:

- take a little time to assure the parents that their infant has no disease.

- explain that crying is the infant's normal means of communication; encourage the parents to listen to it with patience and intelligence.

- convince them that they are perfectly capable of caring for their child without the help of friends, relatives, and neighbors.

- teach them a sensible method of feeding the infant.

Overcoming Feeding Problems

The normal newborn takes frequent small feedings of 1-2 ounces and desires to nurse at short intervals of 1-2 hours, taking as many as 10 to 14 bottles in a 24-hour period. To avoid such frequent feedings, parents often thicken the formula, hoping that the child will be satisfied longer and so require less care. Nothing could be farther from the truth. The best artificial formula is one which approaches the isolevel of mother's milk; to thicken the formula beyond this level produces a metabolic stress on the infant – including his intestinal tract, liver, and kidneys. So, many of the irritable, fussy, so-called colic babies are the result of poor formula construction. Subclinical cases of tetany actually exist in children because of hyperelectrolyte mineral load in unaltered cow's milk feeding.

Then too, there is the question of solid foods. Once it was only with difficulty that parents could be induced to add solid food to the diet of infants. Today, I am alarmed to find what some parents are feeding 2- and 3-week-old infants. Just as there is a normal maturation process for development of neuromuscular achievements, there is a maturation of gastrointestinal function and its readiness to accept solid food. Too early introduction of complex food products can produce irritability and crying in the young infant.

Finally, parents must be encouraged to be flexible in the following of a feeding schedule—feeding the child as much or as little as he desires, as often or as seldom as he desires. Many infants will nurse 3-4 ounces of a formula only to awake screaming ten minutes later. When offered another feeding at this time, the child will take only ½-1 ounce and fall asleep again for four to six hours. To ignore such variations and adhere rigidly to a clock schedule will result in an irritable, screaming baby until the next bottle is due. Remind the parents, too, that there is no sin in taking an infant in the arms, rocking him, and softly singing a lullaby; this has cured more colic than all the "green drops" in the world.

With an understanding by parents that crying is a normal expression of an infant's desires and reactions, with intelligent feeding, with assurance to parents that they are capable of caring for their infant, with intelligent and loving care, we can eliminate forever the fantasy and fiction that colic is an organic entity.

Q. *What about the infant who screams in apparent agony for an hour or so but when given an enema has immediate relief and falls asleep? Is this not a disease state?*

A. Some authors have termed this fairly common condition aerophagy or air-swallowing. At this point I would like to correct a common misconception. Air, which is found in large amounts throughout the infant's gastrointestinal tract, is not due to maldigestion of food. In all instances, any appreciable amount of air is *swallowed* air. This is best prevented by instructing the parent as to "burping" the baby. Sometimes, however, no amount of "burping" will totally prevent air being swallowed and trapped in the bowel to cause distention and discomfort. When this occurs, it is best managed with hot water bottles to the abdomen and, if necessary, a rectal flush.

Q. *What about the infant who is tense, screams out without apparent cause and has hyperactive reflexes? Can this be cured by telling these parents there is no such disease as colic?*

A. Obviously the answer is no. The above described infant has an abnormality which is often called the "hypertonic syndrome." This is a separate disorder that must be removed from the "colic" wastebasket grouping. This condition is usually hereditary. A careful history will usually reveal that one or both parents were themselves or that their brothers or sisters were hypertonic children. On examination one finds a tense, jittery infant with hyperactive reflexes. These infants are a trying problem to parent and doctor alike. We have tried all types of sedatives and tranquilizers on them to no avail. One can only reassure the parents that they have a normal healthy baby and that in due time he will outgrow this condition.

Q. *What about the pacifier? Do you advocate its use in your practice?*

A. About 10 years ago the use of the pacifier was forbidden in most pediatric circles. I too, at that time, tried to discourage its use. However, for those of us who smoke, to deny the existence of "oral gratification" would be sheer hypocrisy. The sucking reflex is an innate reflex and in some babies is much stronger than others. In those in whom nursing does not satisfy the sucking demand, we see no harm in the use of the pacifier.

Q. *What is the ideal formula for an infant?*

A. The ideal feeding is of course breast milk. It is indeed unfortunate that in our society, breast feeding is not in current vogue. An attempt at artificial feeding can best be done by imitation of breast feeding. The caloric strength of breast milk is 20 calories per ounce. Thus our formula should be 20 calories per ounce. The protein-fat-carbohydrate ratio of the artificial formula should approach as nearly as possible the same as breast milk. Formulae should not be varied in strength with age or apparent hunger, because nature has not seen fit to do so with breast milk.

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1. Lemere, F.: Tranylcypromine ('Parnate'), A New Monoamine Oxidase Inhibitor, Am. J. Psychiat. *117*:249 (Sept.) 1960.
2. Petersen, M.C.: Depression: Treatment with a New Antidepressant—Tranylcypromine, report accompanying scientific exhibit at the 116th A.P.A. Meeting, Atlantic City, New Jersey, May 9-13, 1960.
3. Roebuck, B.E., and Maccubbin, H.P.: Treatment of Depression with Tranylcypromine, report accompanying scientific exhibit at the 13th Annual A.M.A. Clinical Meeting, Dallas, Texas, Dec. 1-4, 1959.

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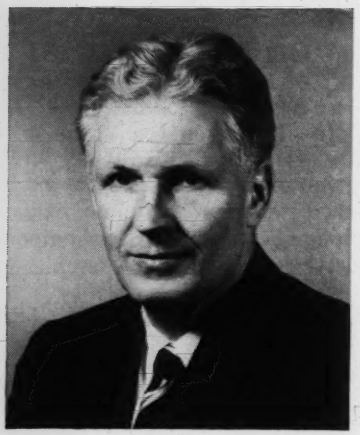
SURGERY



George Crile, Jr., M.D.
Cleveland Clinic

George Crile, Jr., is Head of the Department of General Surgery of the Cleveland Clinic Foundation and Professor of Surgery at the Frank E. Bunts Educational Institute. He received his medical degree at Harvard Medical School, interned at Barnes Hospital of St. Louis University, and took his residency in surgery at the Cleveland Clinic. He is a Fellow of the American College of Surgeons. Dr. Crile has written three textbooks, HOSPITAL CARE OF THE SURGICAL PATIENT, PRACTICAL ASPECTS OF THYROID DISEASE, and CANCER AND COMMON SENSE; in addition, he has published numerous scientific articles, many of them on neoplastic disease, his primary interest.

MINOR SURGERY FOR DISEASES OF THE NIPPLE AND AREOLA

Discharge from the nipple is not a common sign of breast cancer, nor are abscesses or fistulas of areolas signs of underlying malignant disease. Yet mastectomies are occasionally performed for these conditions. Since the loss of a breast should never be a needless loss, I would like to discuss these conditions and show how many of the patients having them can be treated conservatively.

Chronic Cystic Mastitis

Chronic cystic mastitis is the commonest cause of a brownish or opalescent discharge from the nipple. It is not a symptom of cancer. It requires no treatment beyond simple reassurance. Bloody discharge from the nipple, on the other hand, may be associated with intraductal cancer and cannot be disregarded. Brownish discharge of mastitis and the dark discharge due to old blood can be differentiated by microscopic examination of a simple smear. When blood is present, the cytology of the discharge should be studied and the cause of the bleeding investigated. Usually when cytologic examination shows no cancer, the bleeding is due to a papilloma of the duct or intraductal papillomatosis.

Papillomas

The discharge of papillomas of the ducts may be either bloody or serous. If it is serous, it is clear and sparkling, not opalescent like the discharge from mastitis. Usually the discharge due to papilloma, whether serous or bloody,

comes from a single duct and its treatment consists of excision of the duct. Mastectomy is not necessary. Stout's long-range follow-up studies of patients with intraductal papillomas treated by local excision show that there is no higher incidence of cancer in the affected breast than in the unaffected one.

Papillomas can be excised easily by the following method. Under general anesthesia, insert a lacrimal-duct probe into the duct from which the discharge is coming (Figure 1). Make an incision directly across the nipple and areola over the duct. The duct can be raised into the wound simply by lifting the probe; then, using the probe as a guide, the duct can be easily excised. These incisions heal with remarkably little scar or deformity.

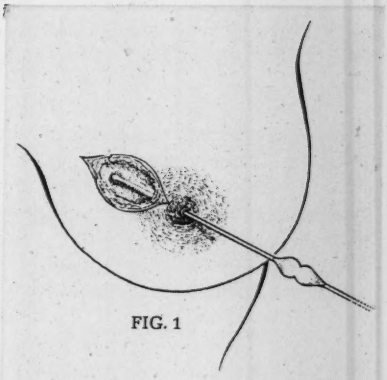


FIG. 1

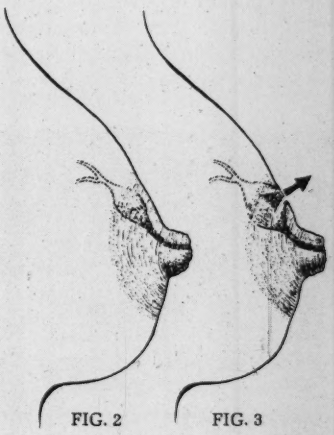


FIG. 2

FIG. 3

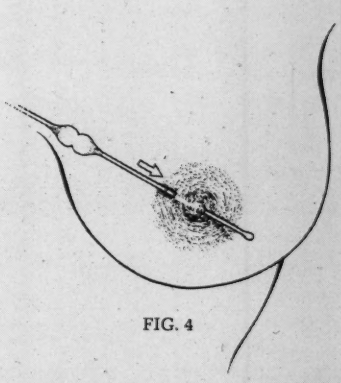


FIG. 4

Squamous Metaplasia

A rare but troublesome type of discharge from the nipple in young women occurs as a result of squamous cell metaplasia in the terminal portion of the lactiferous ducts. The result is a thick white discharge with the consistency of toothpaste, expressible from several ducts, often bilaterally. It has the same sour odor as the contents of a sebaceous cyst. This discharge is composed of squamous epithelial cells desquamated from the terminal portions of the ducts.

Usually squamous metaplasia produces no discomfort and requires no treatment, but sometimes, especially after pregnancy, infections occur. When they do, the clump of dead cells that clog the duct prevents drainage (Figure 2), as in an infected sebaceous cyst. Abscesses form and drain externally through the periphery of the areola (Figure 3), and sometimes per-

sistent drainage produces a fistula between the skin of the areola and the clogged lactiferous duct. Or, if the abscess does heal, it may later reopen or require repeated incisions and drainages. Unfortunately the cause of the condition is not always recognized; without definite treatment, the condition may persist until, in despair, mastectomy is advised. Yet the cause of squamous metaplasia is local and the disease responds to local treatment.

First, under general anesthesia, pass a probe (Figure 4) into the areolar end of the fistula and out the nipple end of the duct. The intervening segment of the duct—the only part ordinarily involved—can then be excised with the probe still in it. The incision is small, running only from the edge of the areola to the opening of the duct. Since the wound is always contaminated, it is best to leave it open. The resulting scar will be scarcely noticeable.

Although the pathology and treatment of squamous metaplasia was reported ten years ago, the disease is still not widely recognized. It is indeed unfortunate when this or any of the minor disorders described here are treated by mastectomy, since an understanding of the pathology of the diseases involved permits conservative management.

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FORMULA: Each tablet contains Benzedrine® Sulfate (brand of amphetamine sulfate), 2.5 mg.; aspirin, 2½ gr. (0.16 Gm.); phenacetin, 2½ gr. (0.16 Gm.). Unlike most analgesic preparations, 'Edrisal' is available on prescription only.
ADMINISTRATION: Two tablets every three hours if needed. Only in exceptional cases will more than six to eight tablets be required in a 24-hour period. For best results, 'Edrisal' should be given about half an hour before eating. In dysmenorrhea, best results are obtained by starting medication two days before menstruation.
In higher dosage ranges, certain individuals may experience some disturbance of sleep if 'Edrisal' is administered in the late afternoon or evening. This, however, can easily be controlled with a mild sedative.
SIDE EFFECTS: Instances of insomnia, excitability and increased motor activity—when they occur—are ordinarily mild, and can be controlled by adjustment of dosage.
CAUTIONS: Use with caution in patients hypersensitive to sympathomimetic compounds; in cases of coronary or cardiovascular disease; and in the presence of severe hypertension.
CONTRAINDICATIONS: Hyperexcitability; agitated pre-psychotic states.
AVAILABLE: In bottles of 50 and 500 tablets.
Prescribing information adopted January, 1961.

INTERNAL MEDICINE

Charles T. Lee, Jr., M.D.
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Charles T. Lee, Jr., is an Associate in Medicine at the University of Pennsylvania School of Medicine and serves on the staff at the Pennsylvania Hospital and Chestnut Hill Hospital. His investigative interest extends to all phases of internal medicine, and has focused on the problems of diabetes. He is co-author of the section on the treatment of diabetes in CURRENT THERAPY 1960; in addition, he served as an editor of a recent issue of MEDICAL CLINICS OF NORTH AMERICA. In addition to the county and state medical organizations, Dr. Lee's professional affiliations include the American College of Physicians and the American Diabetes Association.

DIABETES– A PLEA FOR EARLY TREATMENT

Every now and then, I see a patient with a full-blown (and usually complicated) case of diabetes who mentions that many years ago he had a "trace of sugar in the urine" that his doctor considered harmless. He was told only to reduce the intake of carbohydrates and underwent no further testing – with the ultimate result a severe case of diabetes. Such cases don't need to happen. They can be prevented, or at least delayed, by thorough testing and by continued – relentless – follow-up of the patient's condition.

Great therapeutic sophistication has been achieved in diabetes control in the last three decades. Most of the emphasis has been on control of the blood sugar and treatment of the complications. With the varieties of diets, insulins, and oral agents now available, relatively normal blood-sugar levels can be maintained in almost all cooperative diabetic patients. Unfortunately, controlling the blood sugar does not correct all the metabolic defects of the disease, so diabetic complications, though they may be delayed, continue to occur even in the best controlled patients. Because we have no better therapy at hand, I believe that emphasis in treatment should now shift toward earlier detection. Early detection not only makes for easier control of the disease; it also prevents progression from mild to severe diabetes and prevents or delays complications.

Age As a Factor in Detection and Control

Before considering preventive methods, let me review the three basic kinds of diabetes. The severe, insulin-deficient type develops before the age of 35 and usually has an acute onset. I do not know any way to prevent or delay this type. The most that can be done is to persuade such patients that the better they can control their blood sugar level, the longer they will remain healthy. At the other end of the scale, patients who are 65 and over when diabetes appears do not need or deserve the same intensity of treatment. I think it is useless to engage in frantic dietary contortions to try to prevent or reverse the atherosclerotic changes in these diabetics. Fifty years' accumulation of atheromata will not be overcome by five years of a strict low-fat diet. These patients deserve the best possible control consistent with comfort but without undue restriction of their mode of living.

This leaves a great group of middle-aged patients from which most new diabetics are drawn. About 82% of such patients are markedly overweight; usually, their obesity is chronic and highly resistant to weight-reduction. Unfortunately, good control of diabetes in such patients depends mainly on their ability to follow diets; they are characteristically resistant to insulin, although they can be managed easily if they do lose weight. Here again, we have a problem, though: it is a sad axiom that the longer a person has been fat, the less apt he is to lose weight permanently.

Investigate Glycosuria

A finding of glycosuria, as in the patient I mentioned earlier, almost always suggests diabetes and indicates a necessity for blood-sugar determinations. Glycosuria is important even if found in only one examination, because there is a high probability of mild diabetes. Although glycosuria is continuous in moderate and severe cases, in mild cases it may appear only within 2 hours after a high carbohydrate intake. On the other hand, the absence of glycosuria does not eliminate the possibility of diabetes. In the mildest form of the disease, the diagnosis may have to be made by the glucose-tolerance test.

So, our routine screening for diabetes should include routine urinalysis, preferably on a specimen collected after a meal; postprandial or post-glucose blood-sugar determination in all patients with glycosuria (in mild diabetes, the level of fasting blood sugar is often in the normal range; a more sensitive method is the 2-hour postprandial test after ingestion of a high-carbohydrate meal or 2 hours after 100 gms. of glucose); and, a glucose-tolerance test in patients in whom the previous tests are not conclusive.

A blood-sugar test such as described above should be done every year in any of the following types of patients:

- Anyone with a family history of diabetes—especially when he is obese and/or middle aged. Among 400 apparently healthy, close relatives of diabetics, a 19% incidence of previously unsuspected diabetes and an additional 3.5% incidence of probable diabetes has been found.

- Women with history of pregnancies characterized by: abortions, premature labor, stillbirths, neonatal deaths, or large babies (over 9 pounds).

• Women with glycosuria during pregnancy.

• Patients with transitory glycosuria or non-diagnostic hyperglycemia occurring during surgery, trauma, emotional stress, myocardial infarction, cerebrovascular accident, or administration of adrenal steroids.

• Patients with renal or alimentary glycosuria.

• Patients with symptoms of spontaneous hypoglycemia, especially when there is a positive family history of diabetes.

• Patients with unexplained neuropathy, nephropathy, peripheral vascular disease, or coronary artery disease; unfortunately sometimes only the complications of diabetes lead to its diagnosis. Here is one such familiar tragedy:

> G. F., a 43-year-old colored domestic was admitted to the hospital in August, 1960, with infected gangrene of the first two toes of the right foot. She did not know that she had diabetes, and she had had polyuria and polydypsia for only four months. She weighed 205 pounds on admission but had lost 20 pounds in the past 3 months, and admitted to being obese for at least 25 years. She menstruated normally, had moderate, asymptomatic high blood pressure, and had no known family history of diabetes. The circulation in both legs was poor and all our attempts to control the infection and halt the progression of the gangrene were in vain. A supracondylar amputation was done, following which she made an uneventful recovery. When seen last week in the clinic, she weighed 190 pounds and was hyperglycemic despite taking 40 units of insulin daily.
>
> Considering how frequently diabetes will all but disappear in an obese patient who diets successfully, this case is doubly tragic. If this woman had lost weight between the ages of 18 and 25 and had managed to keep this weight off in the succeeding 15 years, she might not be diabetic now—and almost certainly would still have her leg.

A Second Approach

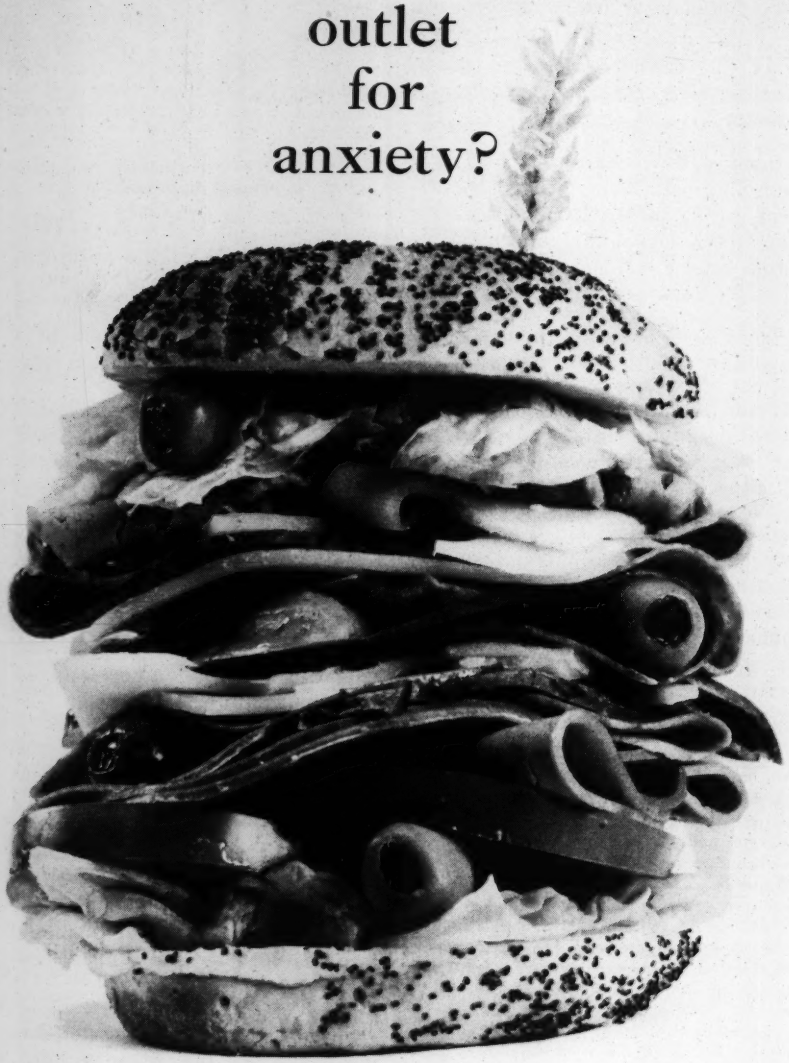
Regular follow-up and thorough testing are only half of the solution. Probably more important is active prevention via dietary control. To wait until the disease appears in a susceptible patient is to wait too long.

Candidates for preventive therapy include the following: fat children and fat adolescents; children or adults with a history of diabetes in the family; women who have either minimal glycosuria during pregnancy or exceptionally heavy babies; and patients with renal glycosuria but an apparently normal glucose tolerance test. All should be impressed again and again with the absolute necessity for maintaining normal body weight.

It is true that patients who could benefit most from preventive treatment are those most reluctant to accept a restricted diet. Nonetheless, obesity is an important factor in the development of diabetes; it is the only metabolic factor in the prediabetic phase which we can control. We should spare no effort to control it, and control it early.

It is easier to change habits and patterns of eating in the 'teens and twenties' than it is in middle age. Our greatest hope for success depends on taking sufficient time to explain to the patient why he must avoid obesity and overeating, and then to re-emphasize this at every subsequent opportunity. With this approach, we may be able to improve some of our present mediocre results in the treatment of diabetes.

outlet for anxiety?



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Kaplan, H.I., et al.: New York J. Med. *57*:2815.

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DERMATOLOGY

Edwin J. Levy, M.D.
University of Pennsylvania

Edwin J. Levy is an Associate in Dermatology at the School of Medicine and the Graduate School of Medicine of the University of Pennsylvania. He received his medical training at Jefferson Medical College, spent eight years in the U. S. Army and in general practice before entering residency training in dermatology at Pennsylvania. He is certified by the American Board of Dermatology and is a member of the American Academy of Dermatology and Syphilology, the Society for Investigative Dermatology, the Philadelphia Dermatologic Society, and the International Society of Tropical Dermatology. Sunlight sensitivity is one of his special interests and has been the subject of several of his articles.

SUNLIGHT SENSITIVITY

Acquiring a nice suntan will be among the goals many vacationers set for themselves this summer. But some may do themselves more harm than good. We know now that the warm summer sunshine, once regarded by physicians and laymen alike as a virtual panacea, may produce many unpleasant and potentially serious reactions in human skin.

Chronic, prolonged exposure to sunlight undoubtedly predisposes to premature aging of the skin. The atrophy, furrowing, and loss of elasticity seen in weather-beaten "sailors' and farmers' skin" are good examples familiar to all. While concern for the possible eventual occurrence of such changes may seem far-fetched to the average sun-enthusiast, there is good evidence that the deleterious effects of the sun are cumulative and at some point they may be irreversible.

Evidence continues to mount that wave lengths of sunlight in the sunburn-reaction zone (2900-3200°A) predispose to skin cancer. Certainly the great majority of premalignant ("actinic") keratoses and skin cancers occur on the exposed surfaces of the face and hands.

Hypersensitivity to sunlight also appears to be a factor in precipitating or exacerbating lupus erythematosus. I recall a patient of mine who was in apparent remission following an attack of subacute systemic lupus erythematosus when, against advice, she spent a day sunbathing at the seashore. Almost immediately, she was stricken with the acute disseminated form of the disease with a rapidly fatal termination.

Of course, sunlight hypersensitivity is not necessarily an essential element in the pathogenesis of all skin cancers and lupus erythematosus; these conditions can also occur in the absence of sunlight. However, there are certain groups of diseases that cannot occur unless there is sunlight. These are the photosensitivity reactions which can be subdivided into phototoxic reactions and photoallergic reactions.

Phototoxic Reactions

Phototoxic reactions are characterized by an intensification of the normal sunburn response, and are dependent upon the presence in the skin of a "photosensitizing agent." In the past few years, there has been an increased incidence of this type of exaggerated sunburn reaction. This has been seen particularly in patients taking certain drugs, notably some of the tranquilizers, broad-spectrum antibiotics, sulfonamides, and newer diuretic agents. Externally applied substances such as coal tars, various dyes, and perfumes containing oil of Bergamot can also produce phototoxic reactions.

The interaction of two factors is required for phototoxicity to develop: a photosensitizing agent, such as a drug, must be present in the prickle-cell layer of the epidermis; the person afflicted must be exposed to a specific source of light, i.e., one that contains wave lengths in the absorption spectrum of the particular photosensitizing agent.

Both of these factors must be present in adequate amounts since each has a threshold concentration that must be reached before phototoxicity will be clinically manifest. For example, I observed that 15 of 64 subjects who took the recommended therapeutic dosage of a new broad-spectrum antibiotic developed a phototoxicity reaction when deliberately exposed to summer sunlight. However, only 2 developed a reaction when the dose was reduced by 25%, and none did when it was reduced to one-half the therapeutic level. Phototoxicity with this drug is not likely to be encountered often, since those who require a dosage large enough to produce this reaction probably would be confined to bed and out of the path of direct sunlight. In another study, with chlorpromazine, 5 of 105 patients developed phototoxicity reactions following exposure to summer sunlight, although all of the 105 had taken the drug for the previous 3 to 8 months without reaction.

In phototoxicity, no increased tolerance can be expected from gradually stepped-up exposures to sunlight or with continued drug administration. Only by avoidance either of the drug or of sunlight can the reactions be prevented in susceptible persons. Although this type of photosensitivity reaction produces no serious consequences, the physical discomfort can be quite distressing. If discomfort is great enough, orally administered steroids usually bring rapid relief and need be continued for just a few days.

Photoallergic Reactions

Photoallergic reactions are characterized by a *qualitatively* altered skin response following sunlight exposure. With them, there is assumed to be an antigen-antibody reaction.

Solar urticaria and eczema solare may be noted in passing, but the more likely photoallergic reaction to be encountered is *polymorphous light eruption*. In this syndrome, papules and slightly elevated small erythematous

plaques appear on exposed portions of the skin, following exposure to wave lengths of sunlight in the sunburn-reaction zone. Lesions resemble the cutaneous manifestations of subacute lupus erythematosus, but no systemic signs (fever, increased sedimentation rate, leukopenia, or positive L.E. test) are present. The eruption subsides within 1-2 weeks if further sunlight exposure is avoided.

Polymorphous light eruption is an acquired disease. Prior to its onset patients react normally to sunlight, but once the pattern is established they respond in this altered fashion.

Antimalarial drugs, such as chloroquine, are effective in the treatment and suppression of polymorphous light eruption. Patients taking one of these drugs can enjoy outdoor activities such as fishing and golfing, and can acquire a normal sunburn and suntan without recurrence of the abnormal eruption. Thus, these drugs cannot be used to prevent normal sunburn and suntan reactions.

The coming of summer, then, should make us increasingly aware of and alert for the possible occurrence of sunlight sensitivity reactions in patients under our care.

QUESTIONS AND ANSWERS

Q. *Isn't sunlight beneficial in some skin conditions?*

A. It may be helpful in patients with acne and psoriasis. Otherwise, its benefits are chiefly psychological: the sense of well being that comes from relaxing in the warm sunshine as well as the pleasing appearance of a nice suntan.

Q. *What actually causes a sunburn?*

A. Exposure to the narrow band of radiation between 2900 and 3200° [the "sunburn-reaction zone"] in the ultraviolet spectrum causes sunburn.

In the northern part of this country, these wave lengths of sunlight reach the earth only in late spring and summer. In winter, when the sun's position is low and toward the horizon, sunlight cannot cause sunburn.

In the South, though, where the wave lengths of sunlight may extend into the sunburn reaction zone most of the year, sunburn can occur in any season.

Q. *Is it advisable to test for porphyrins in all patients with photosensitivity reactions?*

A. I think that it can be safely stated that porphyrins have no role in the production of phototoxicity except in certain types of porphyria. Thus, testing for them can be a needless expense unless other specific clinical indications are present to suggest the diagnosis of porphyria.

Q. *How do you treat a severe, incapacitating sunburn?*

A. In order to provide comfort as quickly as possible, moderate doses of steroids are of great benefit in severe cases. I have found triamcinolone 16 mg. stat., followed by 4 mg. q.i.d. for one day, then t.i.d. the second day, usually sufficient.

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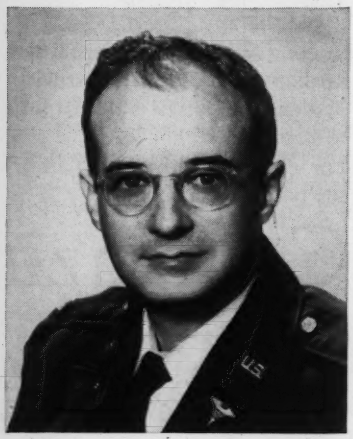
GASTROENTEROLOGY



Eddy D. Palmer, Col., M.C.
Brooke Army Medical Center

Eddy D. Palmer, Col. M.C., has been with the Army since World War II. He is a consultant in gastroenterology to the Surgeon General, and is Chief of the Gastroenterology Section at Brooke Army Medical Center, Fort Sam Houston, Texas. He is Clinical Assistant Professor of Medicine at Baylor University Postgraduate School of Medicine and a member of GP's Editorial Advisory Board. Col. Palmer has written over 200 articles on gastroenterology and is author of four books on gastroenterology, including CLINICAL GASTROENTEROLOGY (Hoeber-Harper).

ABDOMINAL ANGINA:
Symptoms, Signs and Significance

Anyone with a large outpatient practice is no doubt familiar with the thin, undernourished old man who has post-prandial abdominal pain, but no objective signs of disease. Diagnosis is likely to be pancreatic carcinoma, and not until autopsy is it later realized that there was no malignancy but "abdominal angina," as suggested by marked sclerotic narrowing at the origins of the celiac and mesenteric arteries.

By definition, abdominal angina is a syndrome of pain due to ischemia, but, unlike angina pectoris, there is no outspoken relationship between the pathophysiology and the symptom. Of the recognized abdominal arteriosclerotic syndromes, it is probably the most difficult to diagnose with any certainty, and as a consequence its manifestations are easily mistaken for other more common disorders.

Abdominal angina is encountered mainly in men, most often during the seventh and eighth decades, and frequently in those with other sclerotic syndromes, such as stroke residuals or peripheral intermittent claudication. It is characterized by various abdominal pain patterns, which are secondary to muscularis propria ischemia and occur during periods of digestive and absorptive activity in persons with sclerotic gastrointestinal arteries. Three rather distinct pain patterns can be identified as ascribable to abdominal angina, although it

must be emphasized that from patient to patient the symptomatic spectrum is endlessly complex.

Patterns of Pain

The first pain syndrome is both simple and vague. It is probably a valid arteriosclerotic syndrome, but of the three, is the one that most often fails to correlate with the degree of intestinal arteriosclerosis. The patient's complaint is simply one of painful fullness after meals, even small meals. The symptom of quick filling of the stomach is, of course, very common, being indicative merely of an irritable stomach. But the painful sensation is different. It is felt diffusely through the upper abdomen. Very often it is accompanied by nausea, but rarely is there any vomiting. The patient is grouchy and nervous, but not frightened. After about an hour the symptoms clear spontaneously.

The second syndrome is distinctive in that, although the pain comes on only after meals, some physical activity is necessary to bring it on. A common story is that for years the patient has gone out for a walk after supper, but lately during the walk a mild sharp epigastric pain has developed gradually, soon radiating diffusely through the upper half of the abdomen and becoming very severe. The patient feels a need to sit down, whereupon a brief rest brings relief. He then feels well until the next evening.

The third syndrome is by far the most common and, in a sense, most characteristic of the pathophysiology at work. The symptoms begin as a vague mid-abdominal discomfort that is felt soon after especially large meals. The patient is not able to describe the pain specifically, but he often reports that some simple drugstore remedy has helped for a while. Eventually, after several months, the complaint becomes worse, developing into distinct attacks of severe, frightening mid-abdominal pain, which occur after most substantial meals. These attacks, Pal's crises, are specifically periodic and their timing is the syndrome's most characteristic feature. The pain may begin ½-1 hour after eating, then gradually clear spontaneously about two hours later. The interval between the meal and the pain varies considerably from patient to patient, but the pattern, once established, remains remarkably regular.

The pain begins in the center of the abdomen as a deep, heavy ache which is interrupted from time to time by cramps that spread widely through the abdomen. The ache itself radiates to both subcostal areas and posteriorly into the lumbar area. This dull, deep backache is very prominent in some patients, often leading the examining physician to suspect pancreatic carcinoma or to order myelographic studies. The pain is not only severe but also frightening for the patient. He may have the feeling of impending doom and think he may suddenly die at any moment. He may collapse briefly and, in any case, want to lie down. Between attacks the patient feels fine.

Fear of Eating

The patient from the start recognizes the connection between a substantial meal and an attack. He quickly develops a fear of eating, which leads to loss of weight. As time goes on, undernutrition becomes a regular feature of the syndrome; a fat man doesn't remain fat very long if he has severe abdominal angina. In addition to the

fear of eating, a degree of malabsorption from intestinal ischemia often adds to the undernutrition.

Difficulties in Diagnosis

Physical examination does not help establish a specific diagnosis. It will, however, ordinarily show undernutrition and varying degrees of peripheral arteriosclerosis. And in the absence of positive findings, it will lead the examiner to search for a better explanation for the pain. Ordinary x-ray films of the abdomen are of no diagnostic use because the amount of aortic calcification does not necessarily correlate with the degree of sclerotic narrowing of the aortic branches. Aortography effectively demonstrates stenosis of the mesenteric arteries, but, of course, cannot prove the cause of the patient's symptoms. Diagnosis, therefore, depends entirely on the physician's interpretation of the clinical picture.

Management of Distress

Specific treatment is usually a discouraging matter, but several contributions can be made to the patient's comfort. In a small percentage of cases, the nitrites give results as satisfactory as those expected in angina pectoris, suggesting that some degree of arteriospasm occasionally plays a part in narrowing the sclerotic arteries. For the most part, however, they prove ineffective.

In order to encourage the patient to eat, it is necessary to insist on six or eight small meals a day. As simple and reasonable as this step appears to be—and it may give complete symptomatic relief—it frequently proves remarkably difficult to implement. It necessitates a radical change in living habits for an old man, and many old men seem to prefer to suffer rather than to vary their long-established living pattern.

There is an important epilogue to the abdominal angina story. Experience shows that a considerable proportion of patients with abdominal angina eventually go on to develop mesenteric artery occlusion and bowel gangrene, and die. Abdominal angina, in fact, should be considered prodromal of mesenteric artery occlusion. If occlusion is recognized early, surgical arterectomy and graft may prove practicable and life-saving, but it is not thought that the diagnosis of abdominal angina of itself warrants any such radical move.

Next month in CONSULTANT:

Hypogenitalism in Boys: The Case Against "Watchful Waiting"—when to treat underdeveloped boys—and how to prevent the tragedy of irreversible genital immaturity. A practical article by Herbert S. Kupperman, M.D., of New York University.

Cuts and Cusses—suggestions from a plastic surgeon, James T. Metzger, M.D., for improving office treatment of simple lacerations.

Q. *How common is abdominal angina?*

A. It's hard to say since there's a lot of room for diagnostic disagreement about abdominal angina. But, like many diseases of old age it is more common today than it was years ago simply because people are living longer.

Q. *Would the use of estrogens, particularly in male patients, afford any protection against progression of the disease?*

A. One might assume on theoretical grounds that this would be so. But by the time abdominal angina makes itself known, arterial occlusive disease has progressed far. Because of the threat of sudden complete occlusion, the use of estrogens would make good sense, in spite of rather shaky promise of concrete help.

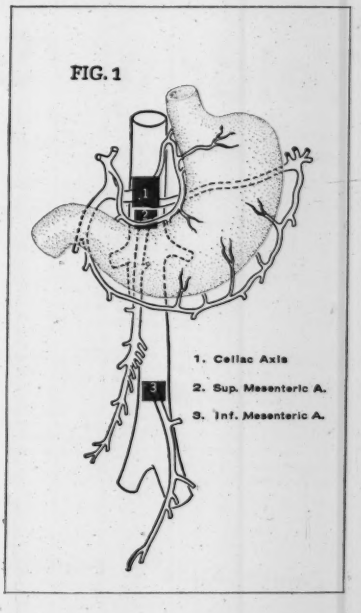
Q. *In view of the good effects of rest on other forms of angina, should one prescribe rest to control pain or painful attacks in abdominal angina?*

A. General physical rest is surprisingly ineffective for prevention and control of abdominal pain in this syndrome. As a matter of fact, since these people tend to be semi-invalid, it's best to encourage physical activity (within their individual limitations, of course) so they can lead as full a life as possible. Resting the gastrointestinal tract, however, is helpful, and as described in my article, is best achieved by replacing the customary three meals a day with a number of smaller ones.

Q. *Is there a correlation between the degree of aortic sclerosis and the severity of celiac and mesenteric arterial disease?*

A. There is no correlation. In fact, nowhere is the myth of arteriosclerosis as a "generalized" disease exposed more convincingly than it is among the visceral arteries. Arteriosclerosis of the gastrointestinal arteries shows a distinct tendency to remain limited to the arterial segment immediately adjacent to the aortic takeoff, no matter how severe it may become there. (See Figure 1.)

FIG. 1



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Rogers, H.L.: Postgrad. Med. *26*:85 (July) 1959.

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PRESCRIPTION SIZE: Bottles of 30 capsules.

Prescribing information adopted January, 1961.

Smith Kline & French Laboratories, Philadelphia

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SPECIAL FEATURE

Harold Brandaleone, M.D.
A.M.A. Committee on Medical Aspects of Crash Injuries and Deaths

Harold Brandaleone has studied motor-vehicle accident prevention both professionally (he serves on 5 committees set up to cope with this problem) and industrially (he served as medical consultant for New York City's Third Avenue Transit Company). He is Chairman of the Industrial Medical Association's Committee on Standards for Motor Vehicle Drivers, Chairman of the National Safety Council's Medical Advisory Committee, and a Member of the AMA's Committee on Medical Aspects of Crash Injuries and Deaths. His other major interests are metabolism and endocrinology; he is past president of the New York Diabetes Association. At New York University College of Medicine, he serves as Assistant Professor of Medicine assigned to Rehabilitation.

WHEN YOUR PATIENT SHOULD STOP DRIVING

The greatest factor in automobile accidents — and one that the physician can influence — is the driver. Poor judgment, faulty attitude, impaired reaction time, emotional disturbance, illness, and physical disability are basic causes of accidents; yet few states have taken steps to locate drivers liable to these handicaps. In Pennsylvania, all drivers will eventually have to pass a medical examination, and all those who are now over 65 must do so to renew their license. In many places, however, it is left pretty much to informal methods, often just voluntary, like the case of the 91-year-old New England woman I read about recently who surrendered her driver's license because she'd decided "things were going too fast nowadays" for her.

No matter how rigid or loose the law is, however, the family physician sometimes finds himself obliged, morally, to persuade his patient to stop driving. It is seldom an easy thing to do, because it may greatly inconvenience the patient to stop driving. So, the physician must consider every aspect of the case before he starts persuading.

First, there are the situational factors to be considered. Does the patient drive mostly on country roads or in heavy traffic? Does he carry passengers? Does he have to drive for long distances? Does he have to drive to earn a living?

Consider Medical Factors

Next there are the medical factors,

the physical disabilities and the diseases that may make driving dangerous. In the table on pages 45 and 46, I have tried to list most of these conditions (you might want to save those pages). In addition, here are a few points that are good to remember in considering whether a patient should stop driving or not.

• Anyone with less than 20/70 corrected vision in the better eye should be advised against driving. The visual field should be 140° or better; a visual field of less than 110° is definitely unsafe because it causes tunnel vision. Color blindness *per se* does not seem to be important, but the ability to see in the dark *is* important and should be evaluated.

• Deafness itself does not keep a person from being a safe driver (deaf persons, conscious of their handicap, are usually especially cautious drivers). Deafness coupled with vertigo, however, suggests internal or middle-ear disturbance, and makes the person unfit for driving.

• With cardiovascular disease, the biggest question is whether the patient is apt to be suddenly incapacitated. Cardiac patients with aortic stenosis, congestive heart failure, carotid sinus syndrome, Adam-Stokes syndrome – or any cardiac condition that might be suddenly incapacitating – should be disqualified.*

• The patient with paralysis after a cerebral-vascular accident should not drive again until his muscular coordination is proven adequate to operate an automobile. Moreover, before the patient drives again, the physician should attempt to determine the likelihood of another stroke.

• Hypertension itself is not disqualifying, but its complications such as damage to the brain, eyes, or kidney may be.

• Most epileptics should not drive. If the patient has been seizure-free for at least 2 years and under careful medical surveillance, he may drive – if he submits to medical examination every few months.

• The brittle or uncontrolled diabetic taking insulin should be advised against driving under any circumstance, since he may develop sudden attacks of hypoglycemia. Patients who can be controlled with diet, or with diet and the oral drugs, however, may be permitted to drive.

Emotional Upset— A Major Cause of Accidents

Finally, there are *emotional* factors, which are probably the most important cause of accidents. Repeated accidents occur most often among drivers who are of low intelligence, youthful, aggressive, or lacking in social responsibility. Many accidents occur among normal drivers because they are temporarily emotionally upset. For example, the driver may have had an argument with his wife, become angry or depressed, and said to himself, "I don't care what happens now." Emotions blunt one's ability to think clearly and interfere with ability to make the continual good judgment

*The following reference material will help you evaluate patients with cardiovascular disease for driving eligibility: *Recommendations for Medical Standards for Motor Vehicle Operators*, Industrial Med. & Surg., January 1957, 26:1, pp. 25-32; *Are You Fit to Drive?*, published by the Committee on Medical Aspects of Automobile Injuries and Deaths, American Medical Association, in cooperation with the Center for Safety Education, Division of General Education, New York University, New York, 1958; *Medical Guide for Physicians in Determining Fitness to Drive a Motor Vehicle*, JAMA 169:1195-1207, (March 14) 1959.

needed in driving an automobile. If the physician has patients who are known to react strongly to emotional problems, they should be advised against driving when they are upset. Psychoneurotics must be evaluated individually; those who are severely depressed or hysterical types are especially prone to accidents and should be dissuaded from driving temporarily.

These are only a few of the things to consider in determining when your patient should stop driving. I have not discussed the roles of alcohol and fatigue in accidents, for they are well known. So are the temporary limitations following surgical operations. The most important thing to remember is that most of your patients drive — and some shouldn't. By being aware of this problem, you can do a great deal to help reduce the tremendous loss of life, disability, and pain that result from motor-vehicle accidents.

QUESTIONS AND ANSWERS

Q. *How about age? When is a person too old to drive?*

A. The ability to drive is determined by physiology, not chronology. A few experienced drivers can continue to drive safely even in their 80's. In general, we believe that people who drive should be given a medical examination every 3 years up to the age of 45 and every 2 years thereafter. The main problem with the older driver is that he may not know new rules and regulations, and he tends to feel that he has been driving for so long that he does not need any re-training, that he knows how to drive better than anyone else on the road.

Q. *What drugs may make a patient unsafe for driving?*

A. Every patient should determine the effects of any new medication before he attempts to drive. The following classes of drugs are especially important, because in some patients they may impair a person's reaction time and alertness: CNS depressants, CNS stimulants, and antihistamines. Small doses of hypnotics, sedatives, and anesthetics may temporarily improve a nervous person's ability to drive, but usually cause depression and drowsiness. Tranquilizing drugs such as meprobamate, chlorpromazine, and reserpine may also produce drowsiness in some patients. Central-nervous system-stimulants such as amphetamine cause temporary alertness and efficiency, but the patient must be cautioned that this effect is only for a short period of time and that he should not expect the medication to keep him awake for prolonged periods. Large doses of such stimulants may cause dizziness, agitation, irritation, and a decreased ability to concentrate. Finally, antihistamines and drugs preventing motion sickness may cause dizziness and drowsiness, and persons taking them should be cautioned against driving until they are sure they are not made drowsy by them. Patients should remember, too, that most cold tablets sold over-the-counter contain antihistamines and, therefore, too, may impair driving ability.

CUT ALONG DOTTED LINE

CUT ALONG DOTTED LINE

MEDICAL CONDITIONS WHICH MAY DISQUALIFY PERSONS FROM DRIVING

GENERAL STATEMENT Any condition that might suddenly incapacitate a person, so that he might be unable to control his senses or his ability to drive a vehicle, is considered disqualifying. Persons with years of driving experience should receive special consideration if their medical defects will not lead to sudden incapacity which might endanger public safety.

Besides the defects listed below, there are several medical problems which should disqualify a motor-vehicle operator:

(1) **Use of drugs:** (a) Narcotics. (b) Sedatives in excess. (c) Antihistamines in excess. (d) Stimulants – excessive or chronic use of Benzedrine or Dexedrine. (e) Drug sensitivity.

(2) **Alcohol:** Chronic or excessive use.
There are some instances where temporary disqualifications occur, e.g., acute or febrile illness, plaster cast, postoperative state; when the acute state is over, the applicant may be reclassified.

HEIGHT AND WEIGHT

No limits.

SKIN

Any chronic skin disease which renders the operator unfit for driving.

Extensive scars which interfere with function.

Cysts or benign tumors of such a size and/or location as to interfere with driving.

HEAD

Deformities of the skull which are symptomatic or associated with underlying disease of the brain, spinal cord or peripheral nerves.

FACE AND NECK

Facial neuralgia, severe.

Torticollis, or spastic contraction of the neck muscle, if severe.

EYES

Monocular vision with less than 20/40 in the other eye.

Visual acuity in each eye less than 20/200 correctible to 20/40.

Any severe active, chronic or progressive disease of the eye.

Marked muscle imbalance and/or astigmatism.

Marked nystagmus.

Diplopia.

Marked impairment of depth perception, glare resistance and defect in visual fields.

EARS

Less than normal spoken voice audible in one ear at 2 feet.

Vestibular disturbance (vertigo).

NOSE AND THROAT

No restrictions.

MOUTH

No restrictions.

THORACIC CAGE

Deformities or scars which decrease cardiac or respiratory function sufficiently to interfere with driving.

EDITOR'S NOTE: *A complete chart, listing also conditions which may make persons ineligible to drive commercial and transportation vehicles, may be obtained upon request. Write to CONSULTANT, SK&F Laboratories, 1500 Spring Garden Street, Philadelphia 1, Pa.*

MEDICAL CONDITIONS WHICH MAY DISQUALIFY PERSONS FROM DRIVING

(cont.)

LUNGS

Any respiratory disease which is disabling.

HEART AND VASCULAR SYSTEM

Severe diminished cardiac reserve.

Congenital heart disease except for minor defects.

Aortic stenosis or combined valvular disease.

Coronary artery disease with anginal syndrome.

Aneurysm of any centrally located or major vessel.

Heart block of significant degree (a slight increase in P-R intervals in the absence of other evidence of heart disease need not disqualify).

Hypertension above 180/100.

Any serious disturbance of rhythm, e.g., auricular fibrillation or flutter.

Orthostatic hypotension if marked and persistent.

Carotid sinus hyperreactivity.

Cerebrovascular disease with or without paralysis.

ABDOMEN AND VISCERA

History of severe gastrointestinal tract bleeding.

GENITOURINARY

Uremia.

VENEREAL DISEASE

Cardiovascular and central nervous system–syphilis.

SPINE AND OTHER MUSCULOSKELETAL

Any disease of bone, muscle or joint which interferes with function.

EXTREMITIES

Any abnormality, deformity or disease which interferes with function.

ENDOCRINE AND METABOLIC

Thyrotoxicosis.

Myxedema or cretinism.

Diabetes mellitus uncontrolled with insulin.

Hyperinsulinism.

BLOOD AND BLOOD-FORMING ORGANS

Any condition which might lead to sudden bleeding and syncope.

PSYCHIATRIC DISORDERS

Psychosis.

Moderate severe chronic psychoneurosis.

Severe transient psychoneurosis (situational).

Marked degree of character, behavior or personality disorder which has prevented good adjustment with particular reference to any antisocial tendencies, overt homosexuality, chronic alcoholism, or drug addiction.

Marked mental deficiency.

Perversion.

NEUROLOGICAL DISORDERS

Neurosyphilis of any form (general paresis, tabes dorsalis, meningovascular syphilis).

Degenerative disorders (multiple sclerosis, encephalomyelitis, cerebellar and Friedreich's ataxia, athetoses, Huntington's chorea, cerebral arteriosclerosis, muscular atrophies, and dystrophies of any type).

Residuals of infection (meningitis and abscesses, paralysis agitans, postencephalitic syndromes, Sydenham's chorea).

Peripheral nerve disorder (chronic or recurrent neuritis or neuralgia of an intensity which is periodically incapacitating, i.e., polyneuritis or neurofibromatosis).

Residuals of trauma (incapacitating residuals of concussion or cerebral trauma, post-traumatic cerebral syndrome, incapacitating injuries to peripheral nerves).

Paroxysmal convulsive disorders and disturbances of consciousness (grand mal, petit mal, psychomotor attacks and narcolepsy).

Miscellaneous disorders (spasmodic torticollis, brain and spinal cord tumors operated and unoperated, cerebrovascular disease, congenital malformations, including spina bifida if associated with neurological manifestations, meningocele even if uncomplicated, and Meniere's disease).

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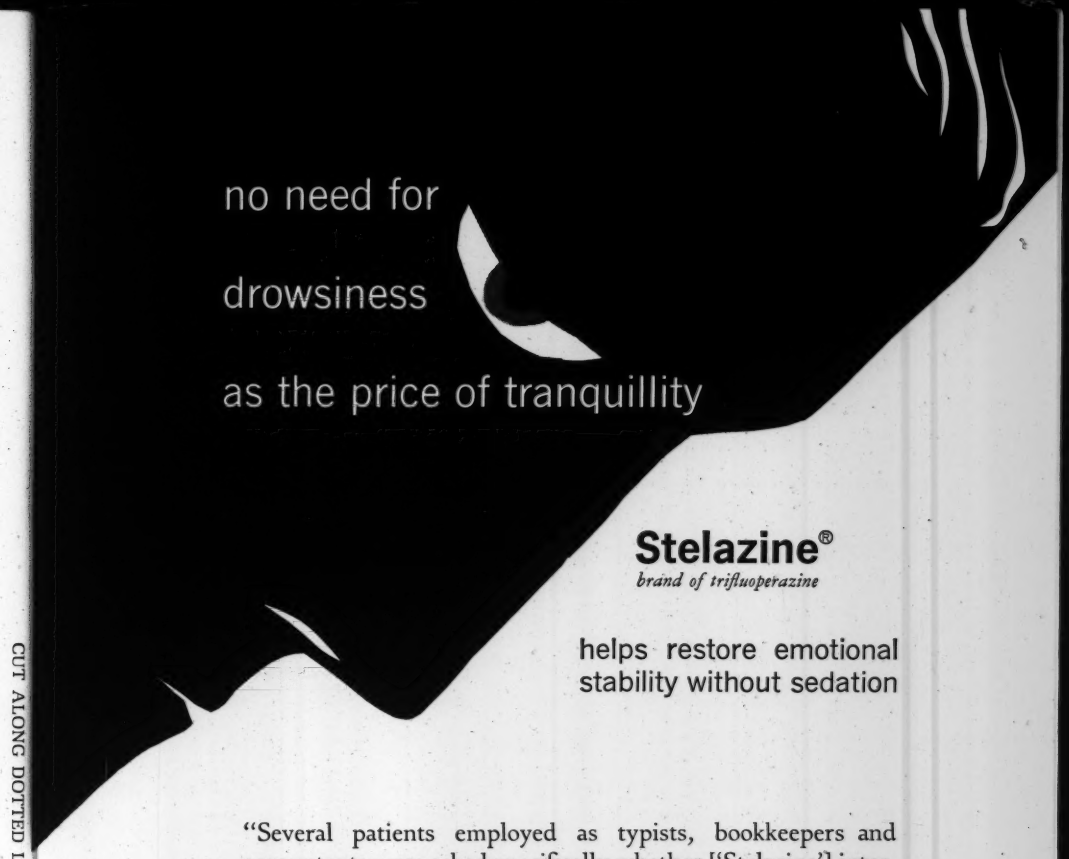
CUT ALONG DOTTED LINE



Stelazine®
brand of trifluoperazine

helps restore emotional stability without sedation

"Several patients employed as typists, bookkeepers and accountants were asked specifically whether ['Stelazine'] interfered with their ability to concentrate; the reply was negative in every instance."[1]

"The particular advantage of 'Stelazine' as compared with many other ataractic drugs is that in low dosage there is almost complete freedom from side effects. . . . The lack of drowsiness and the feeling of alertness commended the drug to patients who could thus continue in their normal occupations."[2]

'Stelazine' has been used as a tranquilizer in more than 2,000,000 patients. A specific anti-anxiety agent, 'Stelazine' works equally well in both *agitated* and *hypoactive* patients.

For complete prescribing information, see back of magazine.

1. Ernst, E.A.: in *Trifluoperazine: Further Clinical and Laboratory Studies,* Philadelphia, Lea & Febiger, 1959, pp. 104-109.
2. Bram, G.: The Treatment of Psychoneurotic Conditions with Trifluoperazine, Brit. J. Clin. Pract. *14*:107 (Feb.) 1960.

SK&F leaders in psychopharmaceutical research

CUT ALONG DOTTED LINE

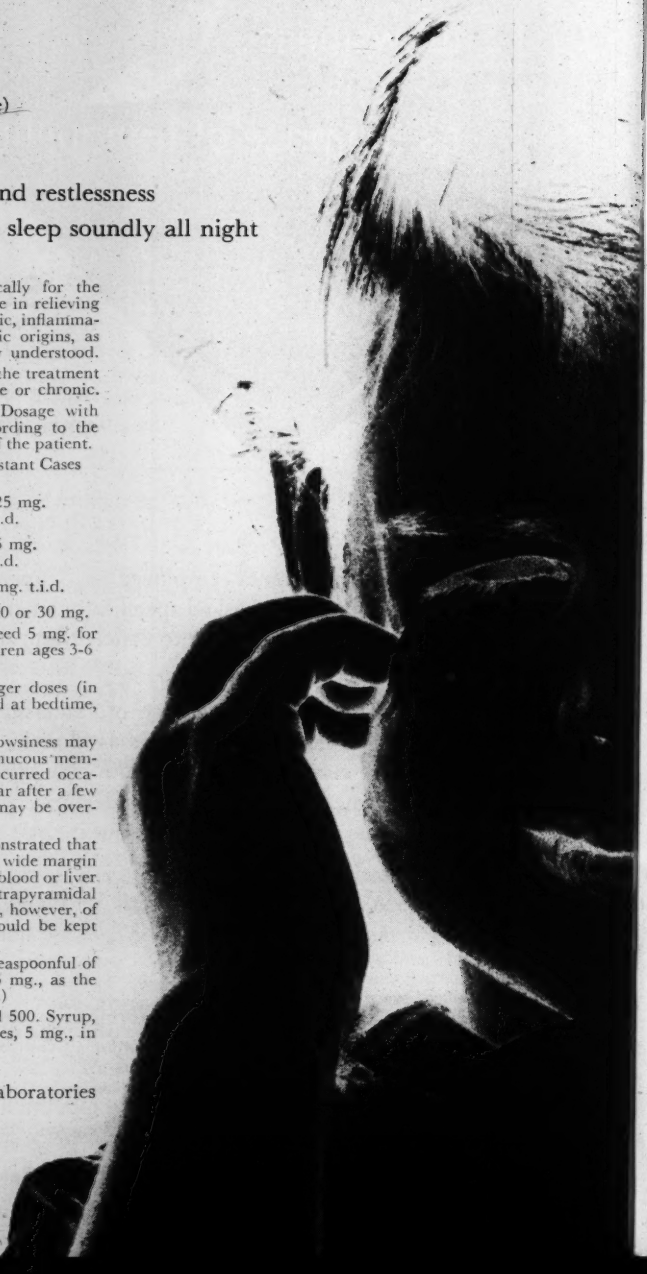
In chickenpox, eczema, urticaria, or other itching disorders in children . . .

Temaril®

brand of trimeprazine (as the tartrate)

stops scratching

- thus reducing irritability and restlessness
- and permitting children to sleep soundly all night



Prescribing Information

'Temaril' is an oral medication specifically for the relief of itching. It has been found effective in relieving pruritus accompanying dermatoses of allergic, inflammatory, metabolic, hemovascular and psychic origins, as well as those whose etiology is not clearly understood.

INDICATION: 'Temaril' is indicated for the treatment of mild and severe pruritus, whether acute or chronic.

DOSAGE AND ADMINISTRATION: Dosage with 'Temaril' should always be adjusted according to the severity of the symptom and the response of the patient.

	Usual Dosage	Resistant Cases
Children		
(ages 2 and under)	1.25 mg. t.i.d.	1.25 mg. q.i.d.
(ages 3-6)	2.5 mg. t.i.d.	2.5 mg. q.i.d.
(ages 7-12)	2.5 mg. t.i.d.	5 mg. t.i.d.
Adults	2.5 mg. q.i.d.	up to 20 or 30 mg.

NOTE: Total daily dosage should not exceed 5 mg. for children ages 2 and under, 10 mg. for children ages 3-6 or 15 mg. for children ages 7-12.

When itching is a nighttime problem, larger doses (in adults: 5 or 10 mg.) should be administered at bedtime, with daytime dosage adjusted accordingly.

SIDE EFFECTS: Mild and temporary drowsiness may be encountered. Dizziness, dryness of the mucous membranes and gastrointestinal upsets have occurred occasionally. All of these effects usually disappear after a few days of medication. Persistent drowsiness may be overcome by reduction of dosage.

CAUTIONS: Clinical experience has demonstrated that 'Temaril', a phenothiazine derivative, has a wide margin of safety and that there is little likelihood of blood or liver toxicity, or neuromuscular reactions (extrapyramidal symptoms). The physician should be aware, however, of their possible occurrence, and patients should be kept under regular observation.

FORMULA: Each tablet and each 5 cc. teaspoonful of 'Temaril' Syrup contains trimeprazine, 2.5 mg., as the tartrate. (The syrup contains alcohol, 5.7%.)

AVAILABLE: Tablets, in bottles of 50 and 500. Syrup, in 4 fl. oz. bottles. Also—Spansule® capsules, 5 mg., in bottles of 30.

SK&F Smith Kline & French Laboratories

Prescribing information adopted January, 1961

THORAZINE®

brand of chlorpromazine

PRESCRIBING INFORMATION

Tranquilizer • Antiemetic • Potentiator

The wide diversity of clinical applications in which 'Thorazine' is valuable, as either a specific or an adjuvant, is due to its three fundamental clinical properties: (1) its capacity to alleviate anxiety, tension and agitation without dulling mental acuity, (2) its ability to potentiate sedatives, narcotics and anesthetics, and (3) its profound antiemetic effect.

The tranquilizing effect of 'Thorazine' accounts for its usefulness in somatic conditions where emotional stress is a factor, as well as in mental and emotional disturbances *per se*.

INDICATIONS

The value of 'Thorazine' is established in the following conditions:

Moderate to severe mental and emotional disturbances of everyday practice, particularly those disturbances marked by agitation, tension, apprehension, excitement, or anxiety.

Somatic conditions complicated by emotional stress, such as arthritis, tuberculosis, severe tension headaches, gastrointestinal disorders, dermatologic conditions, status asthmaticus and severe asthma.

Hospitalized psychiatric patients, to control agitation, dispel delusions and hallucinations, and at the same time to restore or increase the patient's capacity to respond to psychotherapy.

Nausea, vomiting and hiccups, with dramatic results in severe and refractory cases.

Acute or chronic alcoholism, to control agitation, delirium tremens, and nausea and vomiting.

Cancer, as an adjuvant, to control apprehension, suffering due to pain, and nausea and vomiting.

Intractable pain, to reduce suffering and to potentiate narcotics or sedatives.

Obstetrics, as an adjuvant, to control apprehension, pain, and nausea and vomiting. 'Thorazine' allows a reduction in the amounts of the drugs ordinarily used in obstetrical management, thus lessening the risk of respiratory depression in mother and infant.

Surgery, as an adjuvant, to control anxiety and apprehension, pain, and nausea and vomiting; and to reduce by potentiation the amounts of narcotics, sedatives and anesthetics needed.

ADULT DOSAGE AND ADMINISTRATION

Dosage should always be adjusted to the response of the individual and the severity of the condition. It is important to increase dosage until symptoms are controlled or side effects become troublesome.

Mental and Emotional Disturbances of Everyday Practice – Depending on severity, *starting oral dosage* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. After a day or two, dosage may be increased by increments of 20 mg. to 50 mg. daily, at semiweekly intervals (increase should be more gradual in emaciated or senile patients) until achieving maximum clinical response. Continue dosage at this level for at least two weeks; then it can usually be reduced to a maintenance level. A daily dosage of 200 mg. is "average," but in some cases, such as discharged mental patients, daily dosages as high as 800 mg. may be necessary. *Starting intramuscular dose* is 25 mg. (1 cc.). If necessary, and if no hypotension occurs, repeat the initial dose in one hour. Subsequent dosages should be oral, starting at 25 mg. to 50 mg. t.i.d.

Somatic Conditions Complicated by Emotional Stress–*Starting oral dosage* is 10 mg. to 25 mg. t.i.d. or q.i.d. Increase gradually by 10 mg. to 25 mg. increments at semiweekly or weekly intervals. *Starting intramuscular dosage* is 25 mg. (1 cc.), repeated after one hour if necessary and if no hypotension occurs.

Hospitalized Psychiatric Patients – ***Acutely agitated, manic, or disturbed patients:*** *Starting intramuscular dose* is 25 mg. (1 cc.). If no marked hypotension occurs, an additional 25 mg. to 50 mg. injection may be given after one hour. Subsequent intramuscular dosages may be increased gradually over a period of several days – even up to 400 mg. q4-6h in exceptionally severe cases – until the patient is controlled. (In elderly or emaciated patients the dosage should be increased more slowly than in other patients.) Usually the patient becomes quiet and cooperative within 24 to 48 hours after the initial dose, at which time oral doses may gradually be substituted for intramuscular doses (mg. for mg. or higher). Even if control is not complete, oral doses may gradually replace intramuscular doses. During this period, oral dosage should be increased rapidly until the patient is calm. Usually an *oral dose* of 500 mg. a day is sufficient but, if necessary, the dosage may be gradually increased still further to 2,000 mg. a day or higher. ***Less acutely agitated patients:*** *Starting oral dose* is 25 mg. t.i.d. Subsequently, increase the amount gradually until an effective dosage is reached – usually 400 mg. daily is sufficient. ***Duration of therapy:*** It is important to determine the optimal dosage regimen and to continue treatment long enough for maximum clinical response. Maximum improvement is sometimes not apparent until after weeks or even months of therapy.

Nausea and Vomiting – *Starting oral dosage* is 10 mg. to 25 mg. q4-6h, p.r.n., and may be increased if necessary. *Starting intramuscular dose* is 25 mg. (1 cc.). If no hypotension occurs subsequent doses of 25 mg. to 50 mg. q3-4h, p.r.n., may be given until vomiting is checked. Then replace intramuscular administration with oral. *Starting rectal dosage* is one 100 mg. suppository q6-8h, p.r.n. In some patients, one-half this dose may be sufficient.

Hiccups – *Starting oral dosage* is 25 mg. to 50 mg. t.i.d. or q.i.d. If after 2-3 days symptoms persist, *an intramuscular dosage* of 25 mg. to 50 mg. (1-2 cc.) may be used. *Use intravenous administration* only when symptoms still persist. By slow infusion, 25 mg. to 50 mg. (1-2 cc.) should be administered in 500 cc. to 1,000 cc. of physiologic saline solution, with the patient kept flat in bed. Follow blood pressure closely.

Alcoholism – ***Severely agitated patients:*** *Starting intramuscular dose* is 25 mg. to 50 mg. (1-2 cc.). Repeat initial dose if necessary and if no hypotension occurs. Start subsequent oral dosages at 25 mg. to 50 mg. t.i.d. ***Agitated but manageable patients:*** *Starting oral dose* is 50 mg., followed by 25 mg. to 50 mg. t.i.d. ***Ambulatory patients with withdrawal symptoms or sober chronic alcoholics:*** *Starting oral dose* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. Patients in a stuporous condition should be allowed to sleep off some of the effects of the alcohol before 'Thorazine' is administered.

Cancer and Pain – ***Severe pain:*** *starting intramuscular dosage* is 25 mg. (1 cc.) b.i.d. or t.i.d. ***Milder pain:*** starting oral *dosage* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. Because 'Thorazine' potentiates their action, reduce the dosage of narcotics or sedatives to ¼ to ½ of the pre-'Thorazine' level.

Obstetrics – *Intramuscular dose* in labor and delivery is 12.5 mg. to 25 mg. (0.5-1 cc.), administered when dilation of the cervix reaches 3 to 5 centimeters or when strong labor is established. At the same time (but not mixed in the syringe with 'Thorazine'), ¼ to ½ the usual dose of a narcotic or sedative and, if desired, 0.4 mg. of scopolamine may be administered. Depending upon blood pressure, respiration and the general condition of the patient, the initial 'Thorazine' dose (alone or with reduced amounts of the other agents) may be repeated in 3 to 5 hours if necessary.

Surgery (Adults) – ***Preoperatively,*** *oral dose* is 25 mg. to 50 mg., 2 to 3 hours before the operation. *Intramuscular dose* is 12.5 mg. to 25 mg. (0.5-1 cc.), 1 to 2 hours before the operation. ***During surgery*** 'Thorazine' should be administered only if needed to control nausea and vomiting, retching, hiccups, or other acute symptoms. *Intramuscular dose* is 12.5 mg. (0.5 cc.), repeated in ½ hour if necessary and if no hypotension occurs.

Intravenous dose should be no more than 2 mg. per fractional injection, with injections at not less than 2-minute intervals. Also, it should not exceed 25 mg. 'Thorazine' should be diluted to 1 mg./cc. (1 cc. mixed with 24 cc. of physiologic saline solution). ***Postoperatively,*** *oral dosage* is 10 mg. to 25 mg. q4-6h, p.r.n. *Intramuscular dosage* is 12.5 mg. to 25 mg. (0.5-1 cc.), repeated in one hour if necessary and if no hypotension occurs.

PEDIATRIC DOSAGE AND ADMINISTRATION

Nausea and Vomiting, Behavior Disorders and Pain – ***Oral dosage*** is on the basis of ¼ mg./lb. of body weight q4-6h, until symptoms are controlled (i.e., for 40 lb. child—10 mg. q4-6h). Calculate 'Thorazine' Syrup dosage at 10 mg./5 cc. tsp. *Rectal dosage* is on the basis of ½ mg./lb. of body weight q6-8h, p.r.n. (i.e., for 20-30 lb. child—half of a 25 mg. suppository q6-8h). *Intramuscular dosage* is on the basis of ¼ mg./lb. of body weight q6-8h, p.r.n. In children up to 5 years (or 50 lbs.)—not over 40 mg./day. In children 5-12 years (or 50-100 lbs.)—not over 75 mg./day.

Pain—Because 'Thorazine' potentiates the action of narcotics and sedatives, reduce the dosage of these agents to ¼ to ½ of the pre-'Thorazine' level.

Behavior Disorders—In severe cases, 50-100 mg. daily has been used and, in older children, 200 mg. or more daily may be required.

Surgery (Children) – ***Preoperatively,*** dose is on the basis of ¼ mg./lb. of body weight given either orally 2 to 3 hours before the operation, or intramuscularly 1 to 2 hours before. ***During surgery,*** the dose is on the basis of ⅛ mg./lb. of body weight, repeated in ½ hour if necessary and if no hypotension occurs. The intravenous dose should be no more than 1 mg. per fractional injection, with injections at not less than 2-minute intervals. Intravenous dosage during surgery should not exceed recommended intramuscular dosage and should always be diluted to 1 mg./cc. ***Postoperatively,*** dosage is on the basis of ¼ mg./lb. of body weight, either orally q4-6h, p.r.n., or intramuscularly, a single dose repeated in one hour if necessary and if no hypotension occurs.

NOTES ON PARENTERAL ADMINISTRATION

Except for acute ambulatory cases, parenteral administration should generally be reserved for bedfast patients. Parenteral administration should always be made with the patient lying down and remaining so for at least ½ hour afterward because of possible hypotensive effects. The injection should be given *slowly, deep* into the upper outer quadrant of the buttock. If irritation and pain at the site of injection are problems, dilution of 'Thorazine' Injection with physiologic saline solution or 2% procaine solution may be helpful. Subcutaneous administration is not advisable, and care should be taken to avoid injecting undiluted 'Thorazine' Injection into a vein. Intravenous administration is recommended only for severe hiccups and surgery.

Because contact dermatitis has been reported, avoid getting the solution on hands or clothing.

SIDE EFFECTS

The drowsiness caused by 'Thorazine' may be unwanted in some patients. It is usually mild to moderate and disappears after the first or second week of therapy. If, however, drowsiness is troublesome, it can usually be controlled by lowering the dosage or by administering small amounts of dextro amphetamine.

Other side effects that have been reported occasionally are dryness of the mouth, nasal congestion, some constipation, miosis in a few patients and, very rarely, mydriasis. Mild fever (99°F.) may occur occasionally during the first days of therapy with large intramuscular doses. During 'Thorazine' therapy some patients have an increased appetite and gain weight. Usually these patients reach a plateau beyond which they do not gain further weight.

CAUTIONS

Jaundice: In the more than 14 million patients who have been treated with 'Thorazine' in the United States, the incidence of jaundice—regardless of indication, dosage, or mode of administration—has been low. Few cases have occurred in less than one week or after six weeks. Jaundice due to 'Thorazine' is of the so-called "obstructive" type; is without parenchymal damage; and is usually promptly reversible upon the withdrawal of 'Thorazine'. Because detailed liver function tests of 'Thorazine'-induced jaundice give a picture which mimics extrahepatic obstruction, exploratory laparotomy should be withheld until sufficient studies confirm extrahepatic obstruction.

Agranulocytosis: Agranulocytosis, although rare, has been reported in patients on 'Thorazine' therapy. Patients receiving 'Thorazine' should be observed regularly and asked to report at once the sudden appearance of sore throat or other signs of infection. If white blood counts and differential smears give an indication of cellular depression, the drug should be discontinued, and antibiotic and other suitable therapy should be instituted. Because most reported cases have occurred between the fourth and the tenth weeks of treatment, patients on prolonged therapy should be observed particularly during that period.

A moderate suppression of total white blood cells is sometimes observed in patients on 'Thorazine' therapy. If not accompanied by other symptoms, it is not an indication for discontinuing 'Thorazine'.

Potentiation: 'Thorazine' prolongs and intensifies the action of many central nervous system depressants, such as barbiturates and narcotics. Consequently, it is advisable to stop administration of such depressants before initiating 'Thorazine' therapy. Later the depressant agents may be reinstated, starting with low doses, and increasing according to response. Approximately ¼ to ½ the usual dosage of such agents is required when they are given in combination with 'Thorazine'. (However, 'Thorazine' does not potentiate the anticonvulsant action of barbiturates. In patients who are receiving anticonvulsants, the dosage of these agents—including barbiturates—should not be reduced if 'Thorazine' is started. Rather, 'Thorazine' should be started at a very low dosage and increased, if necessary.)

Hypotensive Effect: Postural hypotension and simple tachycardia may be noted in some patients. In these patients, momentary fainting and some dizziness are characteristic and usually occur shortly after the first parenteral dose, occasionally after a subsequent parenteral dose—very rarely after the first oral dose. In most cases, prompt recovery is spontaneous and all symptoms disappear within ½ to 2 hours with no subsequent ill effects. Occasionally, however, this hypotensive effect may be more severe and prolonged, producing a shock-like condition. In consideration of possible hypotensive effects, the patient should be kept under observation (preferably lying down) for some time after the initial parenteral dose. If, on rare occasions, hypotension does occur, it can ordinarily be controlled by placing the patient in a recumbent position with head lowered and legs raised. If it is desirable to administer a vasoconstrictor, 'Levophed' and 'Neo-Synephrine'★ are the most suitable. Other pressor agents, including epinephrine, are not recommended because phenothiazine derivatives may reverse the usual elevating action of these agents and cause a further lowering of blood pressure.

Antiemetic Effect: The physician should always bear in mind that the antiemetic effect of 'Thorazine' may mask signs of overdosage of toxic drugs and may obscure diagnosis of conditions such as intestinal obstruction and brain tumor.

Dermatological Reactions: Dermatological reactions have been reported. Most have been of a mild urticarial type, suggesting allergic origin. Some of them appear to be due to photosensitivity, and it is advisable that patients on 'Thorazine' avoid undue exposure to the summer sun.

Neuromuscular Reactions: With very large doses of 'Thorazine', as frequently used in psychiatric cases over long periods, there have been a few patients who have exhibited neuromuscu-

★'Levophed' and 'Neo-Synephrine' are the trademarks (Reg. U.S. Pat. Off.) of Winthrop Laboratories for its brands of levarterenol and phenylephrine respectively.

lar reactions (extrapyramidal symptoms) which closely resemble parkinsonism. Such symptoms are reversible and usually disappear within a short time after the dosage has been decreased or the drug withdrawn. These neuromuscular reactions can also be controlled by the concomitant administration of standard anti-parkinsonism agents.

Lactation: Moderate engorgement of the breast with lactation has been observed in female patients receiving very large doses of 'Thorazine'. This, however, is a transitory condition which disappears on reduction of dosage or withdrawal of the drug.

CONTRAINDICATIONS

In comatose states due to central nervous system depressants (alcohol, barbiturates, narcotics, etc.), and also in patients under the influence of large amounts of barbiturates or narcotics.

AVAILABLE

Tablets, 10 mg., 25 mg., 50 mg. and 100 mg., in bottles of 50, 500 and 5000; 200 mg., for use in mental hospitals, in bottles of 500 and 5000. (Each tablet contains chlorpromazine hydrochloride, 10 mg., 25 mg., 50 mg., 100 mg., or 200 mg.)

Ampuls, 1 cc. and 2 cc. (25 mg./cc.), in boxes of 6, 100 and 500. (Each cc. contains, in aqueous solution, chlorpromazine hydrochloride, 25 mg.; ascorbic acid, 2 mg.; sodium bisulfite, 1 mg.; sodium sulfite, 1 mg.; sodium chloride, 6 mg.)

Multiple-dose Vials, 10 cc. (25 mg./cc.), in boxes of 1, 20 and 100. (Each cc. contains, in aqueous solution, chlorpromazine hydrochloride, 25 mg.; ascorbic acid, 2 mg.; sodium bisulfite, 1 mg.; sodium sulfite, 1 mg.; sodium chloride, 1 mg. Contains benzyl alcohol, 2%, as preservative).

Spansule® capsules, 30 mg., 75 mg., 150 mg. and 200 mg., in bottles of 30, 250 and 1500; also 300 mg., in bottles of 30 and 1500. (Each 'Spansule' capsule contains chlorpromazine hydrochloride, 30 mg., 75 mg., 150 mg., 200 mg., or 300 mg.)

Syrup, 10 mg./teaspoonful (5 cc.), in 4 fl. oz. bottles. (Each 5 cc. contains chlorpromazine hydrochloride, 10 mg.)

Suppositories, 25 mg. and 100 mg., in boxes of 6. (Each suppository contains chlorpromazine, 25 mg. or 100 mg.; glycerin, glyceryl monopalmitate, glyceryl monostereate, hydrogenated cocoanut oil fatty acids, hydrogenated palm kernel oil fatty acids, lecithin.)

Concentrate (for hospital use), 30 mg./cc., in 4 fl. oz. bottles, packages of 12 and 36; and in 1 gal. bottles. (Each cc. contains chlorpromazine hydrochloride, 30 mg.)

Prescribing information adopted January, 1961

COMPAZINE®

brand of prochlorperazine

PRESCRIBING INFORMATION

Antiemetic • Tranquilizer

'Compazine' provides a beneficial calming effect and prompt antiemetic action with unusual freedom from drowsiness and depressing effect. Clinical experience in several million patients has shown 'Compazine' to be promptly effective in low dosage, with minimal side effects in the dosage range recommended for everyday practice.

INDICATIONS

*1. **Anxiety, tension, agitation,*** confusion, chronic alcoholism and behavior disorders in children.

*2. **Emotional stress associated with somatic conditions*** such as g.i. disorders, cardiovascular conditions, hypertension, menopause, premenstrual tension, neurodermatitis, arthritis, asthma, cancer, tuberculosis and tension headache.

*3. **Nausea and vomiting of widely varying causes*** such as pregnancy, postoperative conditions, viral gastroenteritis and other infectious conditions, irradiation therapy and motion sickness. In most patients, relief is provided within a short time after one oral dose.

*4. **In surgery and obstetrics*** to prevent or control: (a) nausea, vomiting and retching; and (b) fear, tension and restlessness.

*5. **In psychiatry*** to control agitation, anxiety, tension and confusion that may be seen in psychotic states.

ADMINISTRATION AND USUAL DOSAGE

Dosage should be determined according to the severity of the condition and the response of the patient. It is important to begin therapy with the lowest recommended dosage. In hospitalized patients or those under adequate supervision, higher doses may be indicated.

USUAL ADULT DOSAGE

Tablets: The usual starting dosage is 5 mg. three or four times daily. Some patients will respond better when subsequent dosage is raised to 10 mg. t.i.d. or q.i.d. Dosage over 40 mg. daily should be used only in resistant cases.

Spansule® sustained release capsules: The usual starting dosage is one 15 mg. 'Spansule' capsule taken upon arising, or one 10 mg. 'Spansule' capsule in the morning and evening. Some patients may subsequently require dosage increased to one 30 mg. capsule in the morning. Dosage over 40 mg. daily should be used only in resistant cases. (B.i.d. dosage of the 30 mg. capsule should be limited to severe cases.)

Dosage recommendations for other oral forms of 'Compazine' may be applied to 'Compazine' *Spansule* capsules on the basis of the total daily dose in milligrams. (For example: one 15 mg. 'Compazine' *Spansule* capsule replaces 5 mg. 'Compazine' Tablets, t.i.d.) All strengths have the same *duration* of action. They differ only in *intensity* of therapeutic effect.

In "morning sickness" of pregnancy, one 'Compazine' *Spansule* capsule taken before retiring affords antiemetic activity throughout the night and into the morning, thus protecting against "morning sickness."

The 15 mg. 'Compazine' *Spansule* capsule is ideal for once-a-day administration. The 10 mg. 'Compazine' *Spansule* capsule is ideal for twice-a-day (q12h) administration.

Syrup: 5 mg. to 10 mg. (1 to 2 teaspoonfuls) three or four times daily.

Suppositories: Usual dosage in adults is one 25 mg. 'Compazine' Suppository twice daily.

Injection: Total parenteral dosage in 24 hours should not exceed 40 mg.

For intramuscular administration, an initial dose of 5 mg. to 10 mg. (1 to 2 cc.) of 'Compazine' Injection should be injected *deeply* into the upper outer quadrant of the buttock. Repeat, if necessary, at intervals of 3 to 4 hours. Pain at the site of injection has not been a problem. ***For intravenous administration,*** see surgery section. Dilution is not required. ***Subcutaneous administration*** is not advisable because of local irritation.

It is recommended that 'Compazine' Injection not be mixed with other agents in the syringe.

Dermatitis due to contact with 'Compazine' has not been a problem. However, it is recommended that nurses or others giving frequent injections take precautions to avoid getting the solution on their hands or clothing.

'Compazine' Injection should be protected from light, since exposure may cause discoloration. Slight yellowish discoloration will not significantly alter the potency or therapeutic efficacy. However, if markedly discolored, the solution should be discarded.

IN SURGERY (Adults)

ROUTE	DOSAGE
preoperatively	
Intramuscular injection	5 mg. to 10 mg. (1-2 cc.)

1 to 2 hours before induction of anesthesia. Repeat once in 30 minutes if necessary.

ROUTE	DOSAGE
Intravenous injection	5 mg. to 10 mg. (1-2 cc.)

15 to 30 minutes before induction of anesthesia.

Intravenous infusion	20 mg. (4 cc.) per liter of isotonic solution

Add to I.V. infusion 15 to 30 minutes before induction. Repeat once if necessary.

during surgery

Intramuscular or Intravenous injection	5 mg. to 10 mg. (1-2 cc.)

When needed to control acute symptoms. Repeat once if necessary.

postoperatively

To prevent anxiety, nausea, vomiting, or emergence excitement, add to I.V. infusion: 20 mg. (4 cc.) per liter of isotonic solution.

For immediate control of acute nausea, vomiting, retching, or emergence excitement, inject 5 mg. to 10 mg. (1-2 cc.), I.V. or I.M. Repeat once if necessary.

IN OBSTETRICS

'Compazine' dosage should be adjusted to the individual patient and her condition in accordance with the general use of the drug (i.e., 5 mg. to 10 mg. per dose; 15 mg. to 40 mg. per day). The following dosage suggestions should prove satisfactory for the majority of obstetric patients.

To relieve anxiety or prevent vomiting during the first stage of labor, the usual dosage is 10 mg. of 'Compazine' by intramuscular injection. As labor progresses, or if it is prolonged, subsequent 10 mg. doses may be administered as needed. The total daily dose need rarely exceed 30 mg.

To control postpartum anxiety or nausea and vomiting, the usual total daily dose of 'Compazine' is 15 mg. to 30 mg. administered orally or intramuscularly.

NOTE: 'Compazine' has no clinically significant potentiating effect on narcotics, anesthetics, or sedatives. However, because the 'Compazine' patient is calm and relaxed, it is sometimes possible to produce satisfactory analgesia with less than the customary amounts of these agents. This lack of potentiating effect also minimizes the risk of intensifying or prolonging the effect of residual anesthetics and other depressant agents used in surgery or labor and delivery.

As with intravenous administration of any surgical or obstetric adjuvant, the increased possibility of hypotension should be kept in mind if 'Compazine' is administered by either intravenous injection or infusion.

USUAL CHILDREN'S DOSAGE

It is important always to use the lowest effective dosage, because as dosage is raised the possibility of side effects increases. There have been occasional cases of neuromuscular reactions (extrapyramidal symptoms) in children. These have been transitory and reversible.

Nausea and vomiting are usually controlled during the first day of therapy. Therefore more than one day's therapy is seldom necessary.

Weight	Dosage	Not to exceed
Under 20 lbs.	not recommended	
20-29 lbs.	2.5 mg. once or twice a day	7.5 mg. per day
30-39 lbs.	2.5 mg. b.i.d. or t.i.d.	10.0 mg. per day
40-85 lbs.	2.5 mg. t.i.d. or 5 mg. b.i.d.	15.0 mg. per day

For behavior disorders, dosage may be increased gradually, if necessary, within the following daily limits:

2 to 6 years of age: Total daily dose should not exceed 20 mg.
6 to 12 years of age: Total daily dose should not exceed 25 mg.

For rapid control of nausea and vomiting or behavior disorders:

Injection: For children under 12 years of age, each dose should be calculated on the basis of 0.06 mg. of 'Compazine' per pound of body weight and should be administered by deep intramuscular injection. For example, a 40-pound child would receive an injection of 2.5 mg. (0.5 cc.). Control is usually obtained with a single dose.

'COMPAZINE' IN PSYCHIATRY

'Compazine' is indicated for control of agitation, anxiety, tension and confusion that may be seen in such conditions as schizophrenias; manic-depressive states, manic phase; severe personality disorders; involutional psychoses; degenerative conditions; and senile psychoses.

ADULTS

Oral psychiatric dosage: *In relatively mild conditions,* as may be seen in private psychiatric practice or on outpatient clinics, the suggested starting dosage is 5 mg. t.i.d. or q.i.d. Some patients will respond better when subsequent dosage is raised to 10 mg. t.i.d. or q.i.d. *In moderate or severe conditions,* when patients are either hospitalized or under adequate supervision, the suggested starting dosage is 10 mg. t.i.d. or q.i.d. Dosage should be increased gradually until symptoms are controlled or side effects become bothersome. Experience has shown that when dosage is increased gradually (by small increments every two or three days) side effects either do not occur or are easily controlled.

Some patients will obtain satisfactory results on 50 mg. to 75 mg. of 'Compazine' daily. In more severe disturbances, the optimum dosage in most patients is 100 mg. to 150 mg. daily. With oral administration, response ordinarily becomes evident within a day or two. Longer periods of treatment are usually required before maximal improvement is obtained.

I.M. psychiatric dosage: For immediate control of severely disturbed adult patients, an initial dose of 10 mg. to 20 mg. (2-4 cc.) should be injected deeply into the upper outer quadrant of the buttock. If necessary, this dose should be repeated every 2 to 4 hours to gain control of the patient. Patients often respond shortly after the first injection. In resistant cases, the initial dose may be repeated hourly. More than three or four doses are seldom necessary. If, in rare cases, parenteral medication is indicated over a prolonged period, 10 mg. to 20 mg. (2-4 cc.) at 4- to 6-hour intervals is the usual dosage. Pain and irritation at the site of injection have rarely been encountered and some patients have been given the drug intramuscularly for periods of several weeks. After control is achieved by intramuscular administration, most patients can be switched to an oral form of the drug at the same dosage level or higher.

CHILDREN *(2 to 12 years)*

Oral psychiatric dosage: The suggested children's starting dosage in psychiatry is 2.5 mg. (½ teaspoonful of syrup) two or three times daily, or 5 mg. (one teaspoonful of syrup or one 5 mg. tablet) twice daily, according to body weight. During the first day, the total daily dose should not exceed 10 mg. Dosage is then increased according to the patient's response. (2.5 mg. and 5 mg. suppositories are also available.)

For ages 2 to 6, the total daily dosage usually does not exceed 20 mg. *For ages 6 to 12,* the total daily dosage usually does not exceed 25 mg. Because extrapyramidal symptoms have been reported in children as well as in adults, it is important to use the lowest effective dosage.

SIDE EFFECTS

In the dosage range recommended for everyday practice, side effects have been infrequent, transitory and usually mild. A few patients may experience a mild drowsiness when first taking 'Compazine'. There may also be occasional cases of dizziness,

skin reaction and neuromuscular reactions (extrapyramidal symptoms); rarely, hypotension.

Neuromuscular Reactions

Occasionally, neuromuscular reactions (extrapyramidal symptoms) have been observed with 'Compazine' therapy. It is important, therefore, to use the lowest effective dosage, because as dosage is raised the possibility of these reactions increases.

Motor Restlessness: A few patients on 'Compazine'—particularly those in whom dosage has been raised to higher levels—may experience a transient unpleasant stimulation or jitteriness, characterized by restlessness and insomnia. The dosage of 'Compazine' should not be increased while these side effects are present. Patients should be reassured that such effects are temporary and will disappear spontaneously. In those cases where the symptoms are particularly bothersome, reduction of dosage or the concomitant administration of a sedative may be helpful.

Dystonias: These neuromuscular reactions are seen in a significant percentage of hospitalized mental patients on high dosages. The muscles of the face and shoulder girdle may be selectively involved. Symptoms observed have included spasm of the neck muscles, extensor rigidity of back muscles, carpopedal spasm, eyes rolled back, trismus and swallowing difficulty. Despite some similarity to symptoms of serious neurologic disorders, these reactions are usually promptly reversible by temporary discontinuance of 'Compazine' therapy and administration of a sedative such as phenobarbital. The dosage and route of administration should be determined according to the severity of the symptoms. Patients should be reassured that the symptoms are transitory. Depending on the severity of the dystonia, suitable supportive measures, such as maintaining a clear airway and adequate hydration, should be employed. Note: It has been reported that injectable administration of Benadryl* may also be helpful.

Pseudo-parkinsonism: These neuromuscular reactions may resemble the classic parkinsonism syndrome. Treatment should include temporary discontinuance of 'Compazine' therapy and the administration of any standard anti-parkinsonism agent (see *PDR*). Patients should also be reassured that these symptoms are transitory. Depending on the severity of symptoms, suitable supportive measures, such as maintaining a clear airway and adequate hydration, should be employed.

CAUTIONS

Clinical experience has demonstrated that 'Compazine', a phenothiazine derivative, has a wide margin of safety and that there is little likelihood of blood or liver toxicity. The physician should be aware, however, of their possible occurrence.

The antiemetic action of 'Compazine' may mask signs of overdosage of toxic drugs or may obscure the diagnosis of conditions such as intestinal obstruction and brain tumor.

'Compazine' has no clinically significant potentiating action. However, if depressant agents are used in conjunction with this drug, the possibility of an additive effect should be kept in mind.

CONTRAINDICATIONS

'Compazine' is contraindicated in comatose or greatly depressed states due to central nervous system depressants.

AVAILABLE

There is a dosage form of 'Compazine' for every medical need. **Tablets,** 5 mg. and 10 mg. and, for use in psychiatry, 25 mg., in bottles of 50, 500 and 5000. Each tablet contains 5 mg., 10 mg., or 25 mg. of prochlorperazine as the dimaleate.

'Spansule' capsules, 10 mg., 15 mg. and 30 mg., in bottles of 30, 250 and 1500; and, for use in psychiatry, 75 mg., in bottles of 30 and 1500. Each capsule contains 10 mg., 15 mg., 30 mg., or 75 mg. of prochlorperazine as the dimaleate.

Ampuls, 2 cc. (5 mg./cc.), in boxes of 6, 100 and 500. Each cc. contains, in aqueous solution: 5 mg. prochlorperazine as the ethanedisulfonate, 1 mg. sodium sulfite, 1 mg. sodium bisulfite, 8 mg. sodium phosphate and 12 mg. sodium biphosphate.

Multiple-dose Vials, 10 cc. (5 mg./cc.), in boxes of 1, 20 and 100. Each cc. contains, in aqueous solution: 5 mg. prochlorperazine as the ethanedisulfonate, 5 mg. sodium biphosphate, 12 mg. sodium tartrate, 0.9 mg. of sodium saccharin and 0.75% benzyl alcohol as preservative.

Suppositories, 2½ mg. (for young children), 5 mg. (for older children) and 25 mg. (for adults), in boxes of 6. Each suppository contains: 2½ mg., 5 mg., or 25 mg. of prochlorperazine with glycerin, glyceryl monopalmitate, glyceryl monostearate, hydrogenated cocoanut oil fatty acids, hydrogenated palm kernel oil fatty acids and lecithin.

Syrup, 5 mg./teaspoonful (5 cc.), in 4 fl. oz. bottles. Each 5 cc. contains 5 mg. of prochlorperazine as the ethanedisulfonate.

Concentrate (for hospital use), 10 mg./cc. in 4 fl. oz. bottles, cartons of 12 and 36. Each cc. contains 10 mg. of prochlorperazine as the ethanedisulfonate.

Prescribing information also available in *Compazine® Reference Manual, Physicians' Desk Reference,* or from your SK&F representative or your pharmacist.

Prescribing information adopted January 1961.

STELAZINE®

brand of trifluoperazine

PRESCRIBING INFORMATION

INDICATIONS

In general practice and in psychiatry 'Stelazine' is outstanding among tranquilizers because it relieves anxiety, agitation and tension—without sedation. Nor does it cause euphoria. 'Stelazine' is also effective in relieving anxiety either accompanying or causing somatic conditions. Where anorexia and insomnia are problems, 'Stelazine' usually produces a marked improvement in appetite and sleep patterns.

'Stelazine' provides a fast therapeutic response. On a convenient b.i.d. dosage regimen, many patients who have failed to respond to other agents, or have responded only poorly, are promptly relieved of their symptoms. With symptoms allayed, rapport with the physician is facilitated, and patients are more receptive to counselling or psychotherapy.

In hospitalized psychiatric patients 'Stelazine' produces rapid response in many diagnostic categories. These include acute and chronic schizophrenias, manic-depressive psychoses, involutional psychoses, chronic brain syndrome and mental deficiency.

'Stelazine' can combat psychotic symptoms without causing drowsiness. It can quiet hyperactive patients and activate withdrawn patients, and it has a marked beneficial effect on delusions and hallucinations.

'Stelazine' can rapidly terminate acute psychotic episodes. On the admissions service, intensive 'Stelazine' therapy often results in early discharges.

Also noteworthy is the effectiveness of 'Stelazine' in the treatment of hard-core, chronic and refractory schizophrenics. When administered to a group of such patients, it characteristically produces significant improvement in at least 30% to 40% of them.

ADMINISTRATION AND DOSAGE

Dosage of 'Stelazine' should be adjusted to the needs of the individual.

*Trademark Reg. U.S. Pat. Off.: 'Benadryl' for diphenhydramine hydrochloride, Parke-Davis.

1. Adult Dosage for Use in Everyday Practice
Usual starting dosage is 1 mg. twice daily. Optimal dosage is 1 mg. or 2 mg. twice daily. In everyday practice it is seldom necessary to exceed 4 mg. daily.

Because of the inherent long action of 'Stelazine', patients may be controlled on convenient b.i.d. administration; some patients may be maintained on once-a-day administration.

2. Adult Dosage for Use in Psychiatric Practice
oral (for office patients and outpatients with anxiety): The usual starting dosage is 1 mg. b.i.d. In some cases, a better response is achieved on 2 mg. b.i.d. In the treatment of these patients, it is seldom necessary to exceed 4 mg. a day. (Some patients with more severe disturbances, and discharged mental patients, may require higher dosages.) In some patients, maintenance dosage can be reduced to once-a-day administration.

oral (for patients who are either hospitalized or under adequate supervision): The usual starting dosage is 2 mg. to 5 mg. b.i.d. (Small or emaciated patients should always be started on the lower dosage.)

The majority of patients will show optimum response on 15 mg. or 20 mg. daily, although a few may require 40 mg. a day or more. It is important to give doses that are high enough for long enough periods of time – especially in chronic patients.

Optimum therapeutic dosage levels should be reached within two or three weeks after the start of therapy. When maximum therapeutic response is achieved, dosage may be reduced gradually to a satisfactory maintenance level.

intramuscular (for prompt control of severe symptoms): The usual dosage is 1 mg. to 2 mg. (½-1 cc.) by deep intramuscular injection q4-6h, p.r.n. More than 6 mg. within 24 hours is rarely necessary. As soon as a satisfactory response is observed, oral medication should be substituted at the same dosage level or slightly higher.

Only in very exceptional cases should intramuscular dosage exceed 10 mg. within 24 hours. Since 'Stelazine' has a relatively long duration of action, injections should not be given at intervals of less than 4 hours because of the possibility of an excessive cumulative effect.

'Stelazine' Injection has been exceptionally well tolerated; there is little, if any, pain and irritation at the site of injection.

3. Dosage for Psychotic and Mentally Defective Children
The dosages given below apply to children, ages 6 to 12, who are either hospitalized or under adequate supervision.

oral: The starting dosage is 1 mg. administered once a day or b.i.d., depending on the size of the child. Dosage may be increased gradually until symptoms are controlled or until side effects become troublesome. Both the rate and the amount of dosage increases should be carefully adjusted to the size of the child and the severity of the symptoms, and the lowest effective dosage should always be used. Once control is achieved, it is usually possible to reduce dosage to a satisfactory maintenance level.

In most cases, it is not necessary to exceed 15 mg. of 'Stelazine' daily. However, some older children with severe symptoms may require, and be able to tolerate, higher dosages.

intramuscular: There has been little experience with the use of 'Stelazine' Injection in children. However, if it is necessary to achieve rapid control of severe symptoms, 1 mg. (½ cc.) of 'Stelazine' may be administered intramuscularly once or twice a day, depending on the size of the child. Once control is achieved, usually after the first day, the oral dosage forms of 'Stelazine' should be substituted for the Injection.

SIDE EFFECTS

In the dosage range of 2-4 mg. daily, side effects from 'Stelazine' are infrequent. When they do occur, they are usually slight and transitory. Mild drowsiness occurs in a small percentage of patients; this usually disappears after a day or two of 'Stelazine' therapy. There are occasional cases of dizziness, mild skin reaction, dry mouth, insomnia and fatigue; rarely, neuromuscular reactions (extrapyramidal symptoms).

In hospitalized psychiatric patients receiving daily 'Stelazine' dosages of 10 mg. or more, clinical experience has shown that, when side effects occur, their appearance is usually restricted to the first two or three weeks of therapy. After this initial period, they appear infrequently, even in the course of prolonged therapy. Termination of 'Stelazine' therapy because of side effects is rarely necessary.

Side effects observed include dizziness, muscular weakness, extrapyramidal symptoms, anorexia, rash, lactation and blurred vision. Drowsiness has occurred, but has been transient, usually disappearing in a day or two.

Neuromuscular Reactions (extrapyramidal symptoms)
These symptoms are seen in a significant number of hospitalized mental patients receiving 'Stelazine'. They may be characterized by motor restlessness, be of the dystonic type, or they may resemble parkinsonism.

motor restlessness: Some patients may experience an initial transient period of stimulation or jitteriness, chiefly characterized by motor restlessness and sometimes insomnia. These patients should be reassured that this effect is temporary and will disappear spontaneously. The dosage of 'Stelazine' should not be increased while these side effects are present.

If this turbulent phase becomes too troublesome, the symptoms can be controlled by a reduction of dosage or the concomitant administration of phenobarbital or some other barbiturate.

dystonias: These symptoms are rare outside of mental hospitals, but they may be observed occasionally in patients who have received 'Stelazine' as a mild tranquilizer.

Symptoms may include: spasm of the neck muscles, sometimes progressing to torticollis; extensor rigidity of back muscles, sometimes progressing to opisthotonos; carpopedal spasm, trismus, swallowing difficulty, oculogyric crisis and protrusion of the tongue.

The onset of the dystonias may be sudden. A primary characteristic of these symptoms is their intermittency. They may last several minutes, disappear and then recur. There is typically no loss of consciousness and definite prodromata are usually present. Initially, these intermittent symptoms occur in a crescendo of intensity. Then as the effect of the drug wears off, the intervals between the occurrence of symptoms become longer, and the intensity of the symptoms subsides.

Despite their similarity to symptoms of serious neurological disorders, these dystonias are usually promptly reversible and need not cause undue alarm. They usually subside gradually within a few hours, and almost always within 24 to 48 hours, after the drug has been temporarily discontinued.

Treatment is symptomatic and conservative. *In mild cases,* reassurance of the patient is often sufficient therapy. Barbiturates are also useful. *In moderate cases,* barbiturates will usually bring rapid relief. The dosage and route of administration of the barbiturate used should be determined by the intensity of the symptoms and the response of the patient. *In more severe adult cases,* the administration of an anti-parkinsonism agent produces rapid, often dramatic, reversal of symptoms. Also, intravenous caffeine and sodium benzoate seems to be an effective and rapid antagonist to the dystonias. Depending on the severity of the dystonia, suitable supportive measures, such as maintaining a clear airway and adequate hydration, should be employed. *In children,* reassurance and barbiturates will usually control symptoms. Dosage and route of administration should be determined according to the intensity of symptoms and response of patient.

Note: It has been reported that injectable administration of 'Benadryl' may also be helpful in controlling dystonias.

pseudo-parkinsonism: These symptoms are extremely rare outside of mental hospitals.

Symptoms include: mask-like facies; drooling; tremors; pill-rolling motion; and shuffling gait.

Reassurance and sedation are important components of effective therapy. In the majority of cases these symptoms are readily reversible when an anti-parkinsonism agent is administered concomitantly with 'Stelazine'. Occasionally it is necessary to lower the dosage or to temporarily discontinue the drug.

CAUTIONS

Clinical experience has demonstrated that 'Stelazine', a phenothiazine derivative, has a wide range of safety and that there is little likelihood of either blood or liver toxicity. The physician should be aware, however, of their possible occurrence.

One of the results of 'Stelazine' therapy may be an increase in mental and physical activity. In some patients, this effect may

not be desired. For example, although 'Stelazine' has relieved anxiety and, at the same time, anginal pain in patients with angina pectoris, a few such patients have complained of increased pain while taking 'Stelazine'. Therefore, if 'Stelazine' is used in angina patients, they should be observed carefully and, if an unfavorable response is noted, the drug should be withdrawn.

Hypotension has not been a problem, but nevertheless adequate precautions should be taken when the drug is used in patients with impaired cardiovascular systems.

The antiemetic action of 'Stelazine' may mask signs of overdosage of toxic drugs or may obscure the diagnosis of conditions such as intestinal obstruction and brain tumor.

Although 'Stelazine' has shown very little potentiating activity, caution should be observed when it is used in large doses in conjunction with sedatives or depressants.

CONTRAINDICATIONS

'Stelazine' is contraindicated in comatose or greatly depressed states due to central nervous system depressants.

AVAILABLE

Tablets, 1 mg. and 2 mg., in bottles of 50, 500 and 5000. (Each tablet contains 1 mg. or 2 mg. of trifluoperazine as the dihydrochloride.)

For psychiatric patients who are hospitalized or under close supervision:

Tablets, 5 mg. and 10 mg., in bottles of 50, 1500 and 5000. (Each tablet contains 5 mg. or 10 mg. of trifluoperazine as the dihydrochloride.)

Multiple-dose Vials, 10 cc. (2 mg./cc.), in boxes of 1 and 20. (Each cc. contains, in aqueous solution, 2 mg. of trifluoperazine as the dihydrochloride, 4.75 mg. of sodium tartrate, 11.6 mg. of sodium biphosphate, 0.3 mg. of sodium saccharin, and 0.75% of benzyl alcohol as preservative.)

Concentrate (for hospital use), 10 mg./cc., in 2 fl. oz. bottles, in cartons of 4 and 12. (Each cc. contains 10 mg. of trifluoperazine as the dihydrochloride.)

Prescribing information adopted Jan. 1961

PARNATE®

brand of tranylcypromine

PRESCRIBING INFORMATION

The physician should be familiar with the material on dosage, side effects and cautions given below before prescribing 'Parnate', and with the principles of monoamine oxidase inhibitor therapy and the side effects of this class of drugs as reported in the literature. Also, the physician should be familiar with the symptomatology of mental depressions and alternative methods of treatment to aid in the careful selection of patients for 'Parnate' therapy.

INDICATIONS AND LIMITATIONS OF USE

'Parnate' is indicated for the relief of symptoms of mental depression which may include dejected mood, self-depreciation, lowered activity levels, difficulty in making decisions, disturbed eating and sleeping patterns, and variations of these basic symptoms as described in the literature. The therapeutic utility of monoamine oxidase inhibitors is limited specifically to depressive symptoms; these drugs may aggravate some co-existing symptoms such as agitation or anxiety.

In psychiatry, 'Parnate' is indicated in the following diagnostic categories, subject to the limitation stated above: reactive and other psychoneurotic depressions, involutional melancholia, depressive phase of manic-depressive psychosis, psychotic depressive reactions. In the psychiatric treatment of severe endogenous depressions, it is impossible to predict, with presently known data, which patients will respond best to 'Parnate' and which to ECT. 'Parnate' may be indicated in some reactive depressions in which ECT is not indicated. 'Parnate' is not recommended to treat essentially normal responses to temporary situational difficulties.

Note: In depressed patients, the possibility of suicide should always be considered and adequate precautions taken. Exclusive reliance on drug therapy to prevent suicidal attempts is unwarranted, as there may be a delay in the onset of therapeutic effect or an increase in anxiety and agitation. Also, of course, some patients fail to respond to drug therapy.

CLINICAL EXPERIENCE

Extensive clinical trials with 'Parnate' have confirmed its effectiveness and versatility. As always in the evaluation of drugs for psychic disorders, some variation in efficacy has been reported.

These studies provide the following data on the effectiveness and fundamental properties of 'Parnate':

1. In 500 patients on whom complete data are available for statistical analysis, marked or moderate improvement was reported in 77% of the nonpsychotic patients. Marked improvement was reported in 40% and moderate improvement in 27% of the psychotic patients. Some investigators have pointed out that improvement in certain instances, particularly in milder cases, may have been due to spontaneous remission of symptoms.
2. Improvement is seen within 48 hours to three weeks after starting 'Parnate'; the response can be accelerated by using higher than standard initial dosages.
3. 'Parnate' acts primarily as an antidepressant rather than as a euphoriant. Patients feel essentially normal on 'Parnate' therapy.
4. 'Parnate' can facilitate psychotherapy by increasing the patient's willingness to exert mental effort and reducing symptom-centered preoccupations.
5. 'Parnate' appears to prevent relapses in some patients who have been treated initially with ECT.

DOSAGE

Dosage should be adjusted to the requirements of the individual patient. Dosage increases should be made only in increments of 10 mg. per day and ordinarily at intervals of one to three weeks. Side effects occur more often as dosage is increased.

Reduction from peak to maintenance dosage may be desirable before withdrawal. If withdrawn prematurely, original symptoms will recur. No tendency to produce rebound depressions of greater intensity has been seen with 'Parnate', although this is a theoretical possibility in patients treated at high dosages. Experimental work indicates that inhibition of monoamine oxidase persists for only a few days after withdrawal. Thus, any side effects due to this inhibition will probably recede rapidly upon withdrawal, which should be a distinct advantage of 'Parnate' therapy when the patient exhibits poor tolerance to antidepressant medication.

Because there is a striking relationship between dosage and speed of response, two dosage schedules are provided:

A. Standard dosage. (This schedule will not always produce prompt results, but it will hold the incidence of side effects to a minimum.)

1. Recommended starting dosage is 20 mg. per day — administered 10 mg. b.i.d. (morning and afternoon).
2. Continue this dosage for two to three weeks.
3. If no signs of a response appear, increase dosage to 30 mg. daily—20 mg. upon arising and 10 mg. in the afternoon.
4. Continue this dosage for at least a week.
5. As soon as a satisfactory response is obtained, dosage may usually be reduced to a maintenance level.
6. Some patients will be maintained on 20 mg. per day; many will need only 10 mg. daily.
7. If dosages above 30 mg. daily are desired for use in exceptionally resistant cases, refer to the schedule of intensive dosage.

B. Intensive dosage (for accelerated response). (This schedule is for use in hospitalized patients or those under comparable supervision whenever a prompt effect is more desirable than a relative absence of side effects.)

1. Recommended starting dosage is 30 mg. per day. Administer 20 mg. in the morning and 10 mg. in the afternoon.
2. Continue this dosage for one week.
3. If no signs of a response appear, increase dosage gradually at intervals of several days to one week.
4. Dosages above 60 mg. per day are not advisable.
5. As soon as a satisfactory response is obtained, dosage may usually be reduced gradually to a maintenance level.
6. Some patients may be maintained on 20 mg. per day; many will need only 10 mg. daily.

Note: When ECT is being administered concurrently, 10 mg. b.i.d. can usually be given during the series, then reduced to 10 mg. daily for maintenance therapy.

SIDE EFFECTS

A. At standard dosages. Side effects in patients treated with standard doses of 'Parnate' are qualitatively the same as seen at higher dosages but are generally less frequent and less severe.

The patient may experience restlessness, overstimulation, or insomnia; may notice some weakness, drowsiness, episodes of dizziness, or dry mouth; or may report nausea, diarrhea, abdominal pain, or constipation. Occasionally, headaches have occurred. Symptoms of postural hypotension have been seen most commonly, but not exclusively, in patients with pre-existent hypertension; blood pressure returns to pretreatment levels rapidly upon discontinuation of the drug. Other side effects which might occur in rare instances are tachycardia, urinary retention, significant anorexia, skin rashes, edema, palpitations, blurred vision, tinnitus, chills, paresthesia, muscle spasm and tremors, impotence, sweating and possibly paradoxical hypertension.

Most of these side effects can usually be relieved by lowering the dosage or by giving suitable concomitant medication.

B. At intensive treatment dosages. When 'Parnate' is used for intensive treatment to control symptoms more rapidly, an increase in the incidence and severity of side effects must be anticipated.

At doses above 30 mg. daily, postural hypotension is a major side effect of 'Parnate' therapy. It affects largely the systolic readings and occurs mainly, but not exclusively, in patients with a history of hypertension. Rare instances of syncope have been seen. Dosage increases should be made more gradually in patients showing a tendency toward hypotension at the starting dose. Postural hypotension can be relieved by having the patient lie down until blood pressure returns to normal.

Other side effects which may occur are listed above under *standard dosages*. Headaches have occasionally been severe and incapacitating. Overstimulated behavior, which may include increased anxiety, agitation and manic symptoms, can be evidence of either a side effect or an excessive therapeutic action; if this occurs, reduce dosage or administer a phenothiazine tranquilizer.

CAUTIONS

Extensive clinical and laboratory work has shown that there is little likelihood of blood or liver toxicity. Since 'Parnate' is a non-hydrazine compound, it should prove to be exempt from the toxic effects on the liver thought to be due to the hydrazine moiety of some other drugs. However, severe toxic reactions have occurred with some monoamine oxidase inhibitors. Pending further clinical experience, 'Parnate' should probably not be used in patients with a history of liver disease or in those with abnormal liver function tests. Drug-induced jaundice is often difficult to differentiate from other jaundice. However, there has been sufficient clinical experience with 'Parnate' to demonstrate that, if it has any potentiality for producing jaundice, the reaction must be rare. Also, the usual precautions should be observed in patients with impaired renal function since there is a possibility of accumulative effects in such patients.

Although 'Parnate' has been used in combination with various drugs (particularly Stelazine®, brand of trifluoperazine), some monoamine oxidase inhibitors have been reported to have marked potentiating effects on certain drugs, e.g., sympathomimetics, central nervous system depressants, hypotensive agents and alcohol. Therefore, the physician should bear in mind the possibility of a lowered margin of safety when 'Parnate' is combined with potent drugs and should adjust dosage carefully. 'Parnate' should not be used in combination with imipramine. (The reaction of a patient who attempted suicide with a deliberate overdosage of 'Parnate' and imipramine was more severe than would have been predicted from the properties of either drug.)

CASES REQUIRING SPECIAL CONSIDERATION

Administer with caution to patients with recent myocardial infarction or coronary artery disease with angina of effort. Increased physical activity and, more rarely, hypotension have been reported. The pharmacologic properties of 'Parnate' suggest that it may have a capacity to suppress anginal pain that would otherwise serve as a warning sign of myocardial ischemia. When 'Parnate', like any agent which lowers blood pressure, is withdrawn from patients who tend to be hypertensive, blood pressure may again rise to undesirable levels.

When 'Parnate' is combined with a phenothiazine derivative or other compound known to affect blood pressure, elderly patients and those with cardiovascular inadequacies should be observed more closely because of the possibility of additive hypotensive effects.

In patients being transferred to 'Parnate' from another monoamine oxidase inhibitor or from imipramine, allow a medication-free interval of one week, then initiate 'Parnate' using half the normal dosage for at least the first week of therapy. Similarly, a few days should elapse between the discontinuance of 'Parnate' and the administration of another monoamine oxidase inhibitor or of imipramine.

Because the influence of 'Parnate' on the convulsive threshold is variable in animal experiments, suitable precautions should be taken if epileptic patients are treated.

AVAILABLE

Tablets, 10 mg., in bottles of 50 and 1500. (Each tablet contains 10 mg. of tranylcypromine, as the sulfate.)

Prescribing information adopted Feb. 1961

ESKATROL® SPANSULE®

brand of sustained release capsules

PRESCRIBING INFORMATION

FORMULA

Each 'Eskatrol' *Spansule* sustained release capsule contains Dexedrine® (brand of dextro amphetamine sulfate), 15 mg., and Compazine® (brand of prochlorperazine), 7.5 mg., as the dimaleate, distributed among hundreds of minute pellets with varying disintegration times. A therapeutic dose is released immediately and the remaining medication, released slowly and without interruption, sustains the effect for 10 to 12 hours.

INDICATION

'Eskatrol' *Spansule* capsules are indicated in overweight patients, particularly in those who depend on eating for psychologic release.

'Eskatrol' *Spansule* capsules provide not only daylong control of appetite but also relief from the emotional stress associated with overeating and with dieting. The desire to eat is reduced and patients, particularly the so-called "compulsive eaters," feel better and are able to adjust to the weight-reducing program—*even for prolonged periods of time.*

RECOMMENDED DOSAGE

One 'Eskatrol' *Spansule* capsule daily, taken in the morning.

SIDE EFFECTS

Side effects (chiefly nervousness and insomnia) are infrequent, and usually mild and transitory.

CAUTIONS

Clinical experience has demonstrated that 'Eskatrol' (containing the phenothiazine derivative, 'Compazine') has a wide margin of safety and that there is little likelihood of blood or liver toxicity or neuromuscular reactions (extrapyramidal symptoms). The physician should be aware, however, of their possible occurrence.

'Eskatrol' *Spansule* capsules should be used with caution in the presence of severe hypertension, advanced cardiovascular disease, or extreme excitability.

AVAILABLE

In bottles of 30 and 250 capsules.

Prescribing information adopted Jan. 1961

In hay fever and other seasonal allergies . . .

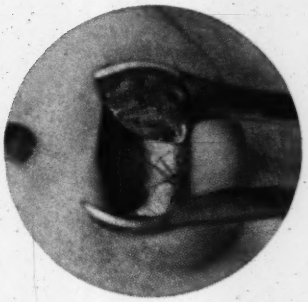
ORNADE® SPANSULE®

brand of sustained release capsules

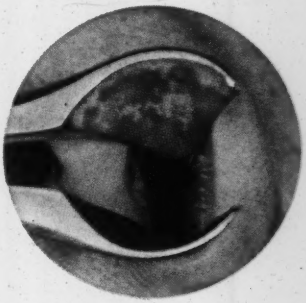
the unique oral nasal decongestant with a special drying agent

relieves sneezing—weeping—nasal congestion

for 24 hours with just two doses daily



Before taking 'Ornade'



2 hours after taking 'Ornade'

PRESCRIBING INFORMATION

The comprehensive formula of 'Ornade' *Spansule* capsules contains a special drying agent, isopropamide iodide, in addition to a decongestant and an antihistamine. Isopropamide iodide acts to reduce excessive weeping and nasal and paranasal secretions. The decongestant, phenylpropanolamine, reduces vascular engorgement and often permits blocked sinus cavities to drain. The antihistamine, 'Teldrin', reduces sneezing, rhinorrhea and itching of the eyes. Acting together, additively, these three agents combine to provide outstanding relief from upper respiratory distress.

INDICATIONS: 'Ornade' *Spansule* capsules are recommended for prompt and prolonged relief from respiratory tract congestion and hypersecretion associated with:

allergic rhinitis:
hay fever
"rose fever," etc.
the common cold
acute, subacute and chronic sinusitis
influenza
vasomotor rhinitis
postnasal drip

DOSAGE (adults and children over 6): For all-day, all-night relief, one 'Ornade' *Spansule* capsule q12h. When taken at bedtime, 'Ornade' keeps patients symptom-free throughout the night and usually enables them to wake up in the morning uncongested and with airways free.

FORMULA: Each 'Ornade' *Spansule* sustained release capsule contains 8 mg. of Teldrin® (brand of chlorpheniramine maleate) and 50 mg. of phenylpropanolamine hydrochloride, so prepared that a therapeutic dose is released immediately and the remaining medication, released slowly and without interruption, sustains the effect for 10 to 12 hours; and 2.5 mg. of isopropamide, as the iodide. Because isopropamide iodide is inherently long-acting, it has not been necessary to put it into sustained release form; therefore, the entire dose of isopropamide iodide is released upon ingestion.

SIDE EFFECTS: Drowsiness, "nervousness," or insomnia may occur on rare occasions, but are usually mild and transitory.

CAUTIONS AND CONTRAINDICATIONS: Use with caution in the presence of severe hypertension. 'Ornade' should not be used in patients with glaucoma or prostatic hypertrophy.

AVAILABLE: 'Ornade' *Spansule* capsules are available in bottles of 30 and 250.

Prescribing information adopted January, 1961.

Smith Kline & French Laboratories

SK&F